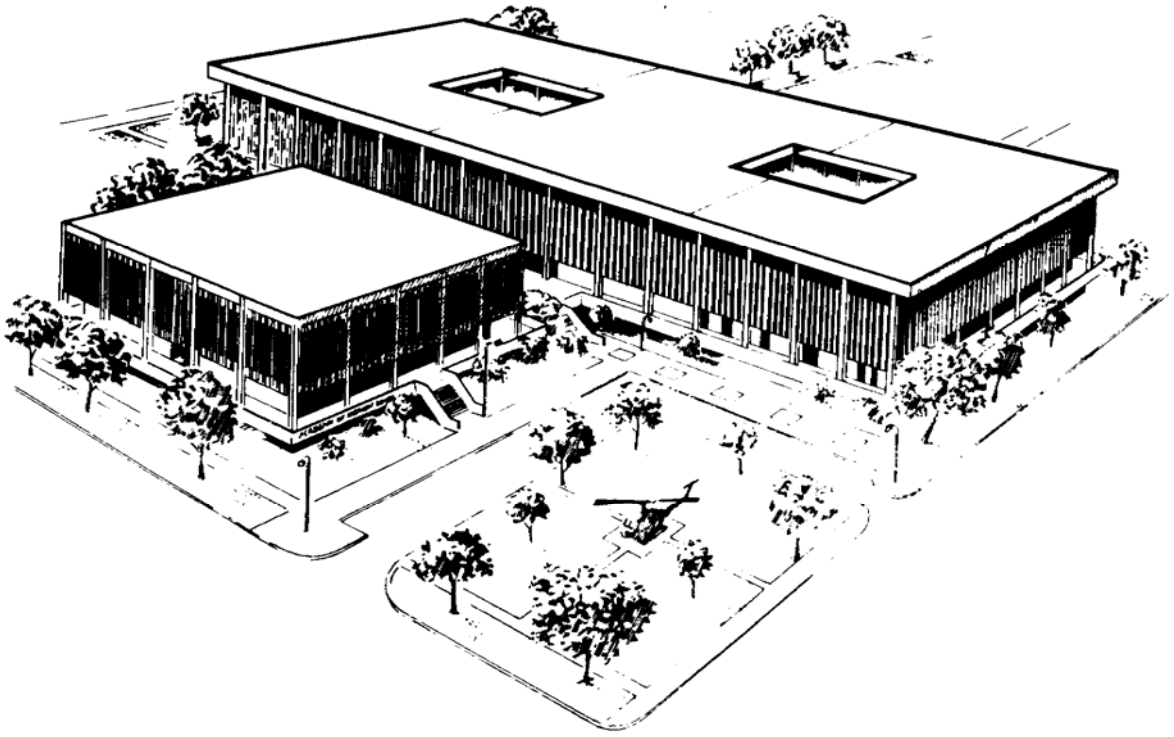
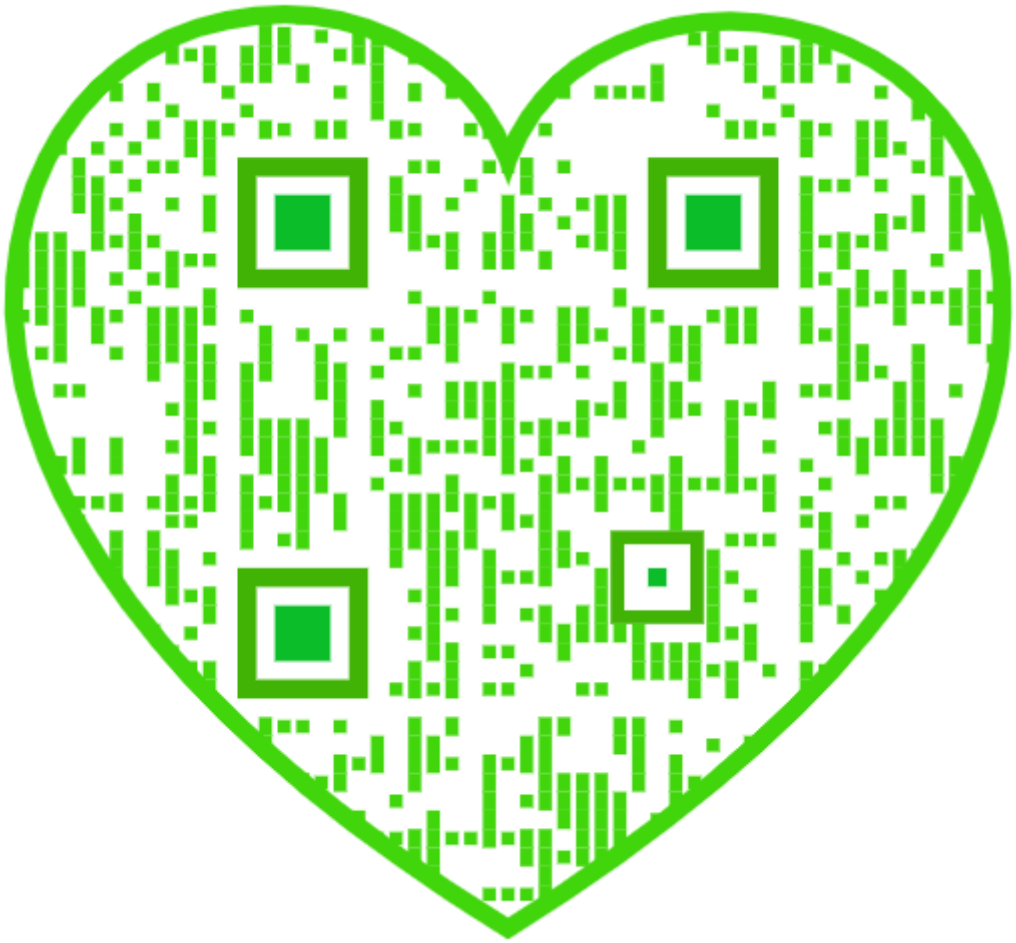
U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL
FORT SAM HOUSTON, TEXAS 78234-6100



PHARMACOLOGY V

SUBCOURSE MD0808 EDITION 100



DEVELOPMENT

This subcourse is approved for resident and correspondence course instruction. It reflects the current thought of the Academy of Health Sciences and conforms to printed Department of the Army doctrine as closely as currently possible. Development and progress render such doctrine continuously subject to change.

ADMINISTRATION

Students who desire credit hours for this correspondence subcourse must enroll in the subcourse. Application for enrollment should be made at the Internet website: http://www.atrrs.army.mil. You can access the course catalog in the upper right corner. Enter School Code 555 for medical correspondence courses. Copy down the course number and title. To apply for enrollment, return to the main ATRRS screen and scroll down the right side for ATRRS Channels. Click on SELF DEVELOPMENT to open the application; then follow the on-screen instructions.

For comments or questions regarding enrollment, student records, or examination shipments, contact the Nonresident Instruction Branch at DSN 471-5877, commercial (210) 221-5877, toll-free 1-800-344-2380; fax: 210-221-4012 or DSN 471-4012, e-mail accp@amedd.army.mil, or write to:

NONRESIDENT INSTRUCTION BRANCH
AMEDDC&S
ATTN: MCCS-HSN
2105 11TH STREET SUITE 4191
FORT SAM HOUSTON TX 78234-5064

Be sure your social security number is on all correspondence sent to the Academy of Health Sciences.

CLARIFICATION OF TERMINOLOGY

When used in this publication, words such as "he," "him," "his," and "men" 'are intended to include both the masculine and feminine genders, unless specifically stated otherwise or when obvious in context.

USE OF PROPRIETARY NAMES

The initial letters of the names of some products may be capitalized in this subcourse. Such names are proprietary names, that is, brand names or trademarks. Proprietary names have been used in this subcourse only to make it a more effective learning aid. The use of any name, proprietary or otherwise, should not be interpreted as endorsement, deprecation, or criticism of a product; nor should such use be considered to interpret the validity of proprietary rights in a name, whether it is registered or not.

TABLE OF CONTENTS

Lesson		Paragraphs
	INTRODUCTION	
1	INTRODUCTION TO MICROBIOLOGY	
	Section I. Introduction	1-1--1-2
	Section II. Microorganisms of Importance	1-3--1-8
	Exercises	
2	INTESTINAL PARASITES AND ANTIPARASITIC AGENTS	
	Section I. Introduction	2-1--2-3
	Section II. Antiparasitic Agents	2-4--2-7
	Exercises	
3	ANTIBIOTICS AND SULFONAMIDES	3-1--3-17
	Exercises	
4	ANTIFUNGALS, ANTIHISTAMINES, AND ANTIMALARIAL AGENTS	
	Section I. Antifungals	4-1--4-2
	Section II. Antihistamines	4-3--4-13
	Section III. Antimalarial Agents	4-14--4-15
	Exercises	
5	BIOLOGICALS	5-1--5-13
	Exercises	
6	VITAMINS AND MINERALS	6-1--6-4
	Exercises	

CORRESPONDENCE COURSE OF THE
U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL

SUBCOURSE MD08O8

PHARMACOLOGY V

INTRODUCTION

In Subcourses MD0804, MD0805, MD0806, and MD0807, various concepts of anatomy, physiology, and pathology as they pertain to pharmacology (with emphasis on current drug therapy) were discussed.

In this subcourse, Subcourse MD0808, we shall view a drug in its treatment of specific ailments. We have included a section on biologicals and vitamins and minerals primarily because natural resistance and vitamins and minerals can prevent as well as successfully treat disease, malnutrition, and vitamin deficiencies.

Remember, this subcourse is not intended to be used as an authoritative source of drug information. As you know, new drugs as well as new uses for existing drugs are continuously being discovered through research. This subcourse can serve as a means for your review or initial learning of pharmacological concepts. You are strongly encouraged to use other references to gain additional information that may assist you in performing your job and better serving your patients.

Subcourse Components:

This subcourse consists of 6 lessons:

- Lesson 1, Introduction to Microbiology.
- Lesson 2, Intestinal Parasites and Antiparasitic Agents.
- Lesson 3, Antibiotics and Sulfonamides.
- Lesson 4, Antifungals, Antihistamines, and Antimalarial Agents.
- Lesson 5, Biologicals.
- Lesson 6, Vitamins and Minerals.

Here are some suggestions that may be helpful to you in completing this subcourse:

--Read and study each lesson carefully.

--Complete the subcourse lesson by lesson. After completing each lesson, work the exercises at the end of the lesson, marking your answers in this booklet.

--After completing each set of lesson exercises, compare your answers with those on the solution sheet that follows the exercises. If you have answered an exercise

incorrectly, check the reference cited after the answer on the solution sheet to determine why your response was not the correct one.

Credit Awarded:

Upon successful completion of the examination for this subcourse, you will be awarded 7 credit hours.

To receive credit hours, you must be officially enrolled and complete an examination furnished by the Nonresident Instruction Branch at Fort Sam Houston, Texas.

You can enroll by going to the web site http://atrrs.army.mil and enrolling under "Self Development" (School Code 555).

A listing of correspondence courses and subcourses available through the Nonresident Instruction Section is found in Chapter 4 of DA Pamphlet 350-59, Army Correspondence Course Program Catalog. The DA PAM is available at the following website: http://www.usapa.army.mil/pdffiles/p350-59.pdf

LESSON ASSIGNMENT

LESSON 1	Introduction to Microbiology.
TEXT ASSIGNMENT	Paragraphs 1-1 through 1-8
LESSON OBJECTIVES	After completing this lesson, you should be able to:

1-1. Given a term pertaining to microbiology and a group of statements, select the statement that best defines the term.

1-2. From a group of statements, select the statement that best describes key characteristics of viruses, bacteria, fungi, or protozoa.

1-3. From a group of statements, select the statement that best describes reproductive characteristics of viruses, bacteria, fungi, or protozoa.

1-4. Given the name of a particular disease, select the type of organism that causes that disease (that is, bacteria).

1-5. From a group of statements, select the statement that best describes how bacteria can be classified.

1-6. Given the name of a disease caused by a microorganism and a group of statements, select the statement that best describes that microorganism.

1-7. Given the name of a disease caused by a microorganism and a group of statements, select the statement that best describes that disease.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 1

INTRODUCTION TO MICROBIOLOGY

Section I. INTRODUCTION

1-1. IMPORTANCE OF MICROBIOLOGY

a. Have you ever had a severe case of the flu? Flu is an outbreak of microorganisms. Now, put yourself in the position of the patient who has come to the window of your outpatient pharmacy. The fact is the patient is less concerned with the fact that he has an infection and more concerned with how he is going to get well. Nonetheless, that person and you have a direct interest in the field of microbiology at that moment.

b. Many of the prescriptions you will fill will be for drugs that affect microorganisms. Penicillin, one of the best-known drugs used to fight infection, has saved countless lives. Actually, many individuals who had severe infections before the days of antibiotics died because no drugs were available to help them fight the infections.

c. Infections are very important to the military. In some wars, more lives were lost to diseases caused by microorganisms than were lost to bullets. Individuals who work in the medical laboratory are responsible for identifying the microorganisms that cause disease, while personnel who work in the pharmacy are responsible for dispensing medications to combat these microbes. All members of the Army's health care team must work together in the critical task of microbial infection control.

1-2. DEFINITIONS

Like any field of study, microbiology has certain unique terms. In order to understand texts or journals that pertain to microbiology, you must be familiar with the terminology of the field. The terms below will serve as a foundation for your readings in microbiology. You should consult a good biology or microbiology text to receive an expanded explanation of these and other definitions related to microbiology.

a. **Microbiology.** Microbiology is the study of microorganisms. Scientists who specialize in the study of microbes are called microbiologists.

b. **Microorganism.** A microorganism is an organism that cannot be seen with the unaided eye. That is, you must use a microscope to see microorganisms. In fact, some microorganisms (like viruses) are so small that special electronic instruments called electron microscopes must be used to view them. Bacteria, viruses, protozoa, and molds are some examples of microorganisms. Microorganisms are sometimes called microbes.

c. **Germ.** Germ is a term frequently used by individuals to describe any and all microorganisms.

d. **Virology.** Virology is the scientific study of viruses.

e. **Bacteriology.** Bacteriology is the scientific study of bacteria.

f. **Mycology.** Mycology is the scientific study of fungi.

g. **Parasitology.** Parasitology is the scientific study of parasites and how these organisms affect other organisms. Many parasites can be seen with the unaided eye.

h. **Disease.** A disease is a condition in which there is a malfunction of the body or an interruption from the body's normal state of health.

i. **Pathogen.** A pathogen is a disease-producing microorganism.

j. **Infection.** An infection is a contamination or invasion of any body tissue by a pathogenic organism. When a microorganism invades the tissue of a human, the human may be harmed. Many people who have infections have signs and symptoms that allow physicians to diagnose the condition. The individual with an infection might experience fever and chills, nausea, vomiting, headache, and/or diarrhea. Needless to say, a person who has a severe infection wants his prescription to be filled quickly so he can return to his bed and rest. A patient who has an extremely severe or contagious infection may be hospitalized and given certain antibiotics intravenously.

k. **Toxin.** A toxin is a poisonous substance. Some microorganisms produce toxins that can harm the body. These microbial toxins may be waste products of metabolism or they may be an integral part of the organism. For example, the bacteria that cause diphtheria and tetanus (lockjaw) produce their effects by toxins. Some large plants and animals also produce toxins. There are several types of toxins.

(1) Endotoxins. Some parts of the cell structures of microorganisms are toxins. These toxins are referred to as endotoxins because the substance is inside the cell. An example of a microorganism that produces endotoxins is S. typhosa, the organism that produces typhoid fever.

(2) Exotoxins. Some microorganisms produce toxins that are secreted or diffused from the cell. Corynebacterium diphtheriae is a microorganism that produces diphtheria by the production of an exotoxin.

(3) Enterotoxins. An enterotoxin is a toxin that is absorbed specifically in the gastrointestinal tract. For example, Staphylococcus aureus produces an enterotoxin when it rapidly grows in such foods as milk, salads, and sandwich fillings. When ingested, this enterotoxin may cause the person to vomit, have diarrhea, and have gastrointestinal cramps. This particular enterotoxin is resistant to destruction by heat.

l. **Morphology.** Morphology is the study of form and structure of organisms.

m. **Physiology.** Physiology is the study of the function of organisms.

n. **Etiology.** Etiology is the study of the cause or origin of disease.

o. **Aerobic.** Aerobic organisms require oxygen in order to live.

p. **Anaerobic.** Anaerobic organisms live in an environment in which there is no oxygen.

q. **Facultative Anaerobic.** A microorganism that is a facultative anaerobe can adapt to oxygenless environment if the need arises, but can live and grow where oxygen is present.

r. **Spore.** A spore is a resting stage form of life some microorganisms are able to produce. Spores are very hearty; they are able to endure great extremes in temperature; hence, they are difficult to kill. Once spore encounters favorable conditions for growth, the microbial cell breaks through the protective spore cell wall and grows as a normal cell.

NOTE: Since spores are so resistant to adverse conditions, you must use potent chemicals or moist heat under pressure to kill them.

s. **Micron.** A micron is a unit of measure used to measure the size of microorganisms. A micron is 1/25,400 (0.000039) of an inch or 0.0001 of a centimeter.

Section II. MICROORGANISMS OF IMPORTANCE

1-3. INTRODUCTION

Microorganisms are extremely important in our everyday lives. In some instances, as the production of certain cheeses, the presence of certain microorganisms is greatly desired. In other cases, as spoiling food or bacterial infections, microorganisms are not desirable. In this section, the major types of microorganisms, their characteristics, and the diseases they produce will be discussed.

1-4. VIRUSES

a. **Characteristics.** Viruses are the smallest microorganisms. A virus can only be seen with the aid of an electron microscope. The diameter of the smallest viruses can be as little as 10 millimicrons (or 39/1,000,000,000 of an inch). Because of their size, most viruses can easily pass through filters that would capture bacteria. Fortunately, our bodies generally develop long-lasting immunity against many viruses. Viruses are composed of an outer coat of protein and an inner coat of either DNA (deoxyribonucleic acid) or RNA (ribonucleic acid). Viruses do not cause a disease like most bacteria. Instead, they change the metabolic and reproductive activity of the host cell. This causes necrosis or death of the host cell.

b. **Reproductive Characteristics.** Viruses are <u>obligate intracellular parasites</u>. This means they must be inside a living cell in order to live. Viruses use the substances of that host cell to reproduce since they do not have the internal structures required for life. Basically, the virus "injects" its internal components (that is, DNA or RNA) into the host cell. Then, the metabolism of the host cell is controlled by the virus. After other viruses are produced inside the host cell, the host cell ruptures, and the viruses are released into the environment.

c. **Viruses and Diseases.** Viruses cause many types of diseases. The disease range from the common cold to polio, rabies, and acquired immune deficiency syndrome (AIDS). Influenza (flu) is actually a viral infection. The virus herpes simplex causes cold sores in humans; in rabbits, a herpes simplex infection is fatal. Two strains of herpes simplex exist: one strain produces cold sores and the other strain produces a type of venereal disease that cannot be cured with existing medications. Another species of the same genus, herpes zoster, causes a condition of the skin called <u>shingles</u> (large flakes of skin come off in scales). Some childhood diseases are caused by viruses. Examples include chickenpox (varicella), German measles (rubella), and "red" measles (rubeola). Also, more severe types of diseases, such as smallpox (which has almost been eradicated from the world), poliomyelitis (an inflammation of the gray matter of the spinal cord and brain), rabies, and yellow fever, are caused by viruses. You should remember that German measles (rubella) is especially dangerous for pregnant women since the virus can pass through the placental barrier and cause birth defects.

1-5. BACTERIA

a. **Characteristics.** There are over 2,000 species of bacteria. Bacteria are relatively large in size when compared to viruses. Some large bacteria are 100 microns in length, while many common bacteria are from 5 to 10 microns (5,000 to 10,000 millimicrons) long. Thus, while bacteria are much larger than viruses, a microscope must still be used to observe them. Bacteria are usually unicellular (one-celled). They reproduce by binary fission (a process in which one bacterium divides to form two bacteria). This process of binary fission occurs quickly. In fact, many bacteria reproduce in this way once every 30 minutes. Under ideal conditions, one bacterium can produce at least 4.64 x 1021 bacteria within 24 hours.

b. **Classification of Bacteria.** Bacteria are most commonly classified by their shape and stain characteristics.

(1) Shape. There are four basic bacterial shapes: cocci (round), bacilli (rod-shaped), spirilla (curved rod), and spirochete (corkscrew). See figure 1-1.

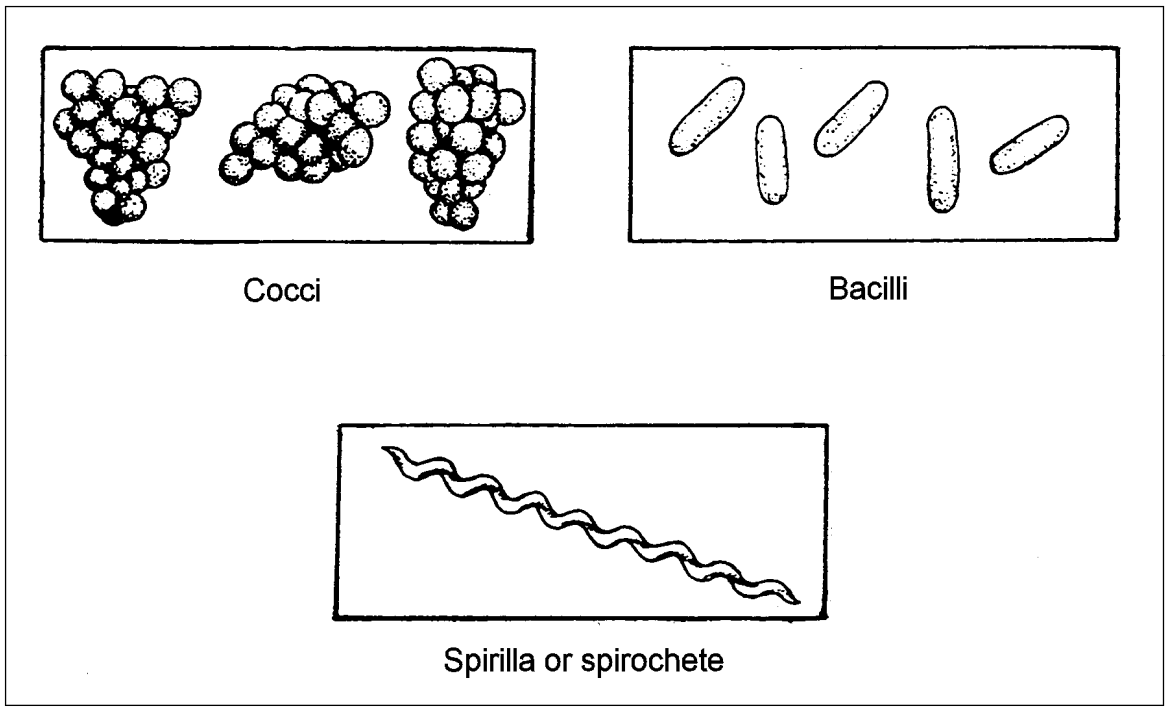


Figure 1-1. The shapes of bacteria

(2) Staining characteristics. There are many staining techniques used in the identification of bacteria. Two commonly used staining procedures are the Gram stain and the acid-fast stain.

(a) Gram stain. This staining technique was developed by Gram, a Danish scientist. Bacteria that are stained a purple color (from crystal violet) are referred to as gram-positive, while bacteria that are stained red (from safranine) are called gram-negative. Interestingly, some gram-positive bacteria are more susceptible to some antibiotics than are some gram-negative bacteria. Thus, this test is important in determining which antibiotic might work against a certain type of bacterial infection.

(b) Ziehl-Neelsen acid-fast stain. This staining technique is used in the identification of the particular types of bacteria responsible for causing tuberculosis and leprosy.

c. **Bacteria and Disease.** Bacteria cause a wide variety of diseases. Many of these are of military significance. Years ago, certain types of bacterial infections meant death to the patient. Today, wise use of antibiotics has given the medical profession one means of combating these types of diseases. One critical factor in dealing with infections caused by bacteria is knowing which bacteria cause a particular disease. This lesson will focus on identifying bacteria and related disease.

(1) Gram-positive bacteria and disease. Staphylococcus is a widespread bacterium that causes minor infections, such as boils and abscesses, and much more severe problems, such as food poisoning and pneumonia. Streptococcus bacteria cause infections such as "strep throat", rheumatic fever, and some upper respiratory infections. The pneumococcus bacterium causes pneumonia. There are several species of Clostridium worth noting. Clostridium botulinum causes the well-known type of food poisoning called botulism (which has about a 60 percent mortality rate). Clostridium tetani causes tetanus (also known as lockjaw). Clostridium perfringens is one of the organisms responsible for causing gas gangrene.

(2) Gram-negative bacteria and disease. This group of bacteria includes such organisms as Escherichia coli, meningococcus, Pseudomonas, Neisseria gonorrhea, Salmonella, Haemophilus influenzae, and Shigella. Escherichia coli is normally found as a major constituent of our intestinal flora. It aids in the breakdown of carbohydrates and helps us absorb vitamin K. This same bacterium can cause urinary tract infections if it enters the urinary system. Since this microorganism is present in human feces, microbiologists can detect the presence of fecal contamination in food and water by determining if Escherichia coli (E. coli) is present in a particular sample. Haemophilus influenzae is a type of bacteria that is commonly found in the throat and nose of many people. It causes bronchopneumonia and sinusitis. This bacterium, however, does not cause influenza; influenza is caused by a virus. Pseudomonas is

commonly found in soil and water samples. This type of bacterium is especially dangerous when it affects the wounds of seriously burned persons. Once established in a burn site, Pseudomonas is difficult to remove. Neisseria gonorrhea is the microorganism that causes gonorrhea. Salmonella is a type of bacterium that frequently causes food poisoning. Salmonella typhi is the organism that causes typhoid fever. This bacterium is especially prevalent in areas that have poor sanitation or in areas affected by a disaster that has resulted in a contaminated water supply. Shigella is a gram-negative bacterium that causes a type of food poisoning.

(3) Acid-fast bacteria. Two bacteria which are acid-fast (that is, stain a particular color in this procedure) are medically important--or at least they were of great concern until modern drugs were used against them. These bacteria are Mycobacterium tuberculosis, the organism that causes tuberculosis and Mycobacterium leprae, the organism that causes Hanssen's disease (leprosy).

(4) Other types of bacteria. Some bacteria are not easily identified by the use of stains. In these instances, special techniques are used to make them visible under the microscope. One of these bacteria is Treponema pallidum, the organism that causes syphilis. This organism is identified by the dark field illumination technique.

1-6. RICKETTSIAS

a. **Characteristics.** Rickettsias (a type of bacteria) are the second smallest microorganisms. That is, rickettsias are larger than viruses, but smaller than most other bacteria. Specifically, the rickettsias range in size from 0.3 micron to 2.0 microns. Rickettsias are found in the alimentary canals of blood-sucking arthropods such as fleas, ticks, lice, and mites. The rickettsias do not form spores and are nonmotile. Once the rickettsias enter the host through the bite of an arthropod, the rickettsias reproduce. The rickettsias are obligate intracellular parasites.

b. **Rickettsias and Disease.** Rickettsias cause only a few types of diseases. Rocky Mountain spotted fever is a well-known disease caused by a certain type of rickettsia. At one time, Rocky Mountain spotted fever was found only in the Rocky Mountain States. The disease has now spread throughout North America. This particular disease is transmitted by ticks. Rocky Mountain spotted fever is characterized by purple blotches over the entire body along with a high-grade fever. Other diseases caused by rickettsias include typhus (both endemic and epidemic) that is transmitted by lice, and Q (Query) fever, which is similar to pneumonia. The role of ticks in the transmission of Q fever is not fully understood.

1-7. FUNGI

a. **Characteristics.** Yeasts and molds are classified under the category of fungi. Fungi range in size from around 3 microns to 20 microns. Fungi are often visible as colonies with the unaided eye. Typically, fungi cause infections on the skin. These infections are not usually serious (for example, life-threatening); however, if a fungal infection becomes systemic, it becomes very difficult for the patient to recover.

b. **Fungi and Disease.** A very common fungal ailment is "athlete's foot", which is caused by Trichophyton mentagrophytes or Epidermophyton floccosum. Ringworm (a fungal infection, not really a worm infestation) can affect both the scalp area and the general body surface. Ringworm is caused by Microsporum canis or Microsporum gypseum. Thrush (also called sprue); a fungal disease characterized by white patches in the mouth and throat is caused by Candida albicans. This condition is common in people who are on chronic antibiotic therapy. Candida infections can also occur in the vagina and urinary tract.

1-8. PROTOZOA

a. **Characteristics.** The protozoa are the smallest animals and the largest microorganisms. You have probably observed some protozoa using a microscope in biology class. These organisms are plentiful in streams and lakes. While most protozoa are harmless to humans, some of these organisms can cause disease.

b. **Protozoa and Disease.** Several protozoa are of key military medical significance.

(1) Trichomonas vaginalis. Trichomonas vaginalis is a small, one-celled protozoan that has several ship-like flagella for locomotion. This organism causes inflammation and a purulent (pus-like) discharge from the vaginal tract in women. It can also cause a urinary tract infection in males. Occasionally, the organism is found in the mouth (leading to gingivitis, inflammation of the gums) and in the intestine (leading to diarrhea). This organism can be transmitted by sexual contact, but it can also be carried on moist clothing or towels. These particular organisms can be killed by drying.

(2) Entamoeba histolytica. Entamoeba histolytica is an organism that causes amebiasis. Amebiasis is primarily restricted to the large intestine. In this disease, the patient experiences inflammation of the colon with diarrhea and watery stools that contain blood, mucus, and pus. This stage of the condition is frequently called amoebic dysentery. Should the intestine become perforated (that is, develop a hole), there will be excessive internal bleeding and infection of the soft tissues of the body (such as the lungs, spleen, liver, and brain). The organism usually enters the host in a cyst form (that is, thick-walled form resistant to environmental changes). Once inside the host, it has the ability to emerge from the cyst (infective stage). The spreading

of the organism inside the body in which tissue is consumed by the organisms is referred to as the invasive stage. Transmission of the cyst is usually made by food handlers in areas of poor sanitation, since the amoeba leaves its host in the cyst form in feces. Perhaps the easiest way to remember the four modes of transmission of Entamoeba histolytica are the "four F's": food, flies, fingers, and feces. It is estimated that over 10 million persons are affected annually in the United States by amebiasis. The last major outbreak of this condition in the US was in 1933 at the Chicago World's Fair. Over 1400 cases (with four fatalities) were reported. While there are over 26 different species of amoebas known to man (several of which live normally within our bodies), only six or seven amoebas actually cause disease in man.

(3) Plasmodium vivax, Plasmodium malariae, Plasmodium falciparum, and Plasmodium ovale. Plasmodium organisms cause malaria. Malaria is one of the prevalent diseases in the world. Fortunately, it is rarely seen in the United States. As of 1965, there were over 300 million new cases and approximately 3 million deaths attributed to malaria. Malaria primarily infects the red blood cells, but it can secondarily infect the liver. The vector (carrier) for malaria is the female Anopheles mosquito. The protozoan lives and reproduces sexually in the female mosquito's gastrointestinal tract. When the mosquito bites a human, the mosquito regurgitates digestive juices into the site of the bite. In this manner, the protozoa are injected into the host's blood, where the protozoa live and reproduce asexually in the host's red blood cells. Because of the life cycle of the protozoa, killing the mosquito vector is the best method of controlling malaria. Symptoms of malaria include sudden chills, fever, and sweating because of destruction of red blood cells. The destruction of the red blood cells can lead to an anemic state which often affects the spleen and liver. There are basically four types of malaria produced by four different species of the protozoan: Plasmodium vivax, Plasmodium malariae, Plasmodium falciparum, and Plasmodium ovale.

(a) Plasmodium vivax causes the most commonly occurring type of malaria. If improperly treated, the patient may have recurring (relapsing) bouts of malaria.

(b) Plasmodium malariae is a relatively rare form of malaria.

(c) Plasmodium ovale causes the rarest form of malaria, which is limited to Western Africa.

(d) Plasmodium falciparum causes the most severe type of malaria, so severe it can lead to death if left untreated. This form of malaria has also been known to cause Blackwater fever, a condition in which red blood cells and the liver are destroyed. Falciparum malaria is also the easiest form of malaria to treat.

Continue with Exercises

EXERCISES, LESSON 1

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. A germ is:

   a. A specific type of microorganism which is known to cause disease.

   b. A virus that is pathogenic to humans.

   c. A term used by many people to describe all microorganisms.

   d. A small creature that is present in the gastrointestinal systems of arthropods.

2. A spore is:

   a. A reproductive form of microorganism (like bacteria).

   b. A resting stage form of life that is capable of enduring undesirable environmental conditions.

   c. A form of microorganism which is very susceptible to heat and chemical conditions.

   d. A stage of growth most microorganisms pass through before they can reproduce.

3. Select the statement that describes a virus.

   a. Viruses are microorganisms that range in size from 5 to 10 microns in length.

   b. Viruses are the second smallest microorganisms.

   c. Viruses are the only microorganisms that are obligate intracellular parasites.

   d. Viruses are microorganisms that have an outer coat of protein and an inner core of either DNA or RNA.

4. Fungi are microorganisms that:

    a. Are obligate intracellular parasites.

    b. Usually cause infections of the skin.

    c. Are the smallest animals and the largest microorganisms.

    d. Frequently cause systemic infections in humans.

5. Protozoa are:

    a. Obligate intracellular parasites.

    b. Composed of an outer coat of protein and an inner core of RNA or DNA.

    c. Microscopic organisms which cause malaria and athlete's foot.

    d. The smallest animals and the largest microorganisms.

6. Bacteria reproduce by:

    a. Binary fission.

    b. Tricking the host cell into duplicating their RNA or DNA.

    c. Injecting their contents into the host cells in order to control the metabolism of the host cells.

    d. The periodic union of male and female bacteria.

7. Influenza is caused by a:

    a. Virus.

    b. Bacteria.

    c. Fungus.

    d. Protozoan.

8. Malaria is caused by a:

   a. Protozoan.

   b. Bacteria.

   c. Virus.

   d. Fungi.

9. Ringworm is caused by a:

   a. Parasitic worm.

   b. Bacterium.

   c. Fungus.

   d. Protozoan.

10. Bacteria can be classified by:

   a. Their size.

   b. Their age.

   c. Their staining characteristics and shape.

   d. The means they use to reproduce.

11. Amebiasis is a condition in which:

   a. There is an inflammation of the colon due to a viral infection.

   b. The patient has diarrhea and watery stools that contain blood, mucus, and pus.

   c. The microorganism causing the infection is carried by the female Anopheles mosquito.

   d. The irritation of the colon occurs either in 48-hour or 72-hour cycles.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 1

1. c (para 1-2c)
2. b (para 1-2r)
3. d (para 1-4a)
4. b (para 1-7a)
5. d (para 1-8a)
6. a (para 1-5a)
7. a (para 1-4c)
8. a (para 1-8b(3))
9. c (para 1-7b)
10. c (para 1-5b)
11. b (para 1-8b(2))

End of Lesson 1

LESSON ASSIGNMENT

LESSON 2 Intestinal Parasites and Antiparasitic Agents.

TEXT ASSIGNMENT Paragraphs 2-1 through 2-7.

LESSON OBJECTIVES After completing this lesson, you should be able to:

2-1. Given an important term pertaining to intestinal parasites, select the statement that best defines the given term.

2-2. Given the scientific name of an intestinal parasite, select the common name corresponding to the given scientific name.

2-3. Given the scientific and/or common name of an intestinal parasite, select the statement that best describes the life cycle, method of infestation, or signs or symptoms associated with the given intestinal parasite.

2-4. From a group of statements, select the statement that best describes the most economical and effective approach to treating parasitic infestations.

2-5. Given the trade or generic name of a drug used to treat intestinal parasite infestations, select the trade or generic name corresponding to the given name.

2-6. Given the trade or generic name of an antiparasitic drug, select the statement that describes the use, caution or warning, or adverse reaction associated with the given drug.

2-7. Given the scientific or common name of an intestinal parasite, select the name (trade or generic) of the agent that should be used to treat an infestation of that intestinal parasite.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 2

INTESTINAL PARASITES AND ANTIPARASITIC AGENTS

Section I. INTRODUCTION

2-1. INTRODUCTION

Throughout recorded history, humans have been infected by parasites, from single cell protozoa to large worms, living in their gastrointestinal systems. Each type of parasite presents certain medical problems as well as economic losses because of disability and loss of productivity. Parasite control is of vital concern to the military. Sanitary procedures can be used to prevent infestation in many cases. In instances in which infestation has occurred, you will be called upon to dispense medications to rid these parasites from the soldiers' bodies.

2-2. IMPORTANT TERMS AND DEFINITIONS PERTAINING TO INTESTINAL PARASITES

a. **Parasitism.** Parasitism is an obligatory relationship in which one organism, the parasite is metabolically dependent on another organism, the host. The host may or may not be harmed by being infested with the parasite.

b. **Normal Flora.** Normal flora consists of microorganisms that are normally found in or on the body in the absence of disease.

c. **Ectoparasite.** An ectoparasite is a parasite that lives on the outer surface of the host.

d. **Endoparasite.** An endoparasite is a parasite that lives inside the host.

e. **Anthelmintic Drug.** An anthelmintic drug is a chemical substance used to eradicate or reduce in numbers helmintic parasites (worms) in the intestinal tract or tissue of a human.

f. **Purge.** A purge is the administration of a cathartic (laxative) to a patient in order to remove parasites from the patient's intestines after the patient has taken an anthelmintic drug. (Anthelmintic agents do not always kill worms in the gastrointestinal tract; some agents only paralyze them. By giving a purge, the worms that are in the intestines can be removed from the gastrointestinal tract).

2-3. INTESTINAL PARASITES OF IMPORTANCE

There are many parasites that can infest the gastrointestinal tract of a soldier. This lesson will discuss some of those parasites.

a. **Entamoeba histolytica** (pronounced EN-tuh-MEE-buh his-toe-LIT-i-kuh)**.** Entamoeba histolytica is a protozoan, a one-celled organism. Using microscopic examination, one stage of the organism looks very similar to the amoeba you have probably observed in some biology classes. Entamoeba histolytica is present throughout the world, but it is found frequently in warm locations that have poor sanitary conditions. The moving, feeding, and reproducing stage of the organism (the trophozoite) lives in the lower gastrointestinal tract of the host. The organism can form a cyst. A cyst is a stage of life that does not move and feed. This is the form of the organism that infects the host. Humans ingest these cysts, which pass through the gastrointestinal tract until they reach the lower intestine. There, the cysts become trophozoites. Additional cysts are then formed and passed from the body in feces. The cysts are spread by ingestion of feces-contaminated material or food. Poor sanitary procedures contribute to the spread of the cysts. Fingers, fluid, flies, and other animal carriers can all carry the cyst-contaminated material. Diseases caused by Entamoeba histolytica include amebiasis, amebic dysentery, and amebic hepatitis (if the liver is infected). Symptoms associated with these conditions include abdominal discomfort, bloody dysentery, diarrhea, and fever.

b. **Trichuris trichiura** (pronounced trick-YOO-ris Trick-ee-YOO-ruh). Trichuris trichiura has the common name of whipworm (see figure 2-1). The whipworm is a parasitic roundworm that lives in the intestines. Humans are the main hosts of this organism. Trichuris trichiura is commonly called a whipworm because it has a whip-like head. The worm can reach a length of 50 mm. Infection is by ingestion of the eggs. The host does not need to ingest any intermediate host. Once ingested, the larva comes out of the eggshell in the upper part of the small intestine, and it remains in the intestines. Eventually it imbeds a part of itself into the intestinal mucosa of the host, where it obtains its nourishment. People who have had a heavy infestation of whipworms usually have the following signs and symptoms: frequent and blood-streaked loose stools, pain and tenderness in the abdomen, severe anemia, and weight loss. Laboratory examination of the patient's stools can lead to a specific identification of whipworm infestation. Infestations may be prevented by the sanitary disposal of human wastes (feces), careful preparation of vegetables, washing of hands before meals, application of principles of personal hygiene, and treatment of persons infested with whipworms.

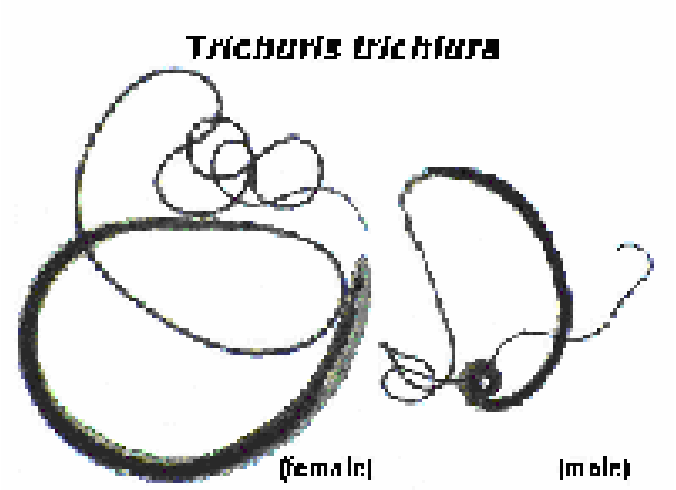


Figure 2-1. Whipworms.

c. **Enterobius vermicularis** (pronounced EN-tur-O-bee-us ver-mick-yoo-LAIR-is). Enterobius vermicularis is frequently referred to as the pinworm (see figure 2-2). This roundworm is small; females are usually 8 to 13 mm long and males are usually 1 to 5 mm in length. Humans are the only known host of pinworms. After the host ingests the pinworm eggs, the eggs hatch in the small intestine. The worms then develop and begin the reproductive cycle. The females leave the large intestine to deposit their eggs (up to 11, 000) in the perianal area of the human body. Pinworms usually live in the intestines, but they can travel to the stomach, esophagus, and nose. Pinworm infestations are common, especially in children. Since the eggs are not usually laid in the intestine, stool examinations for purposes of worm identification are usually ineffective. A piece of clear cellophane tape with the sticky side applied around the anus in the morning before the patient has washed or defecated, can be used to gather samples for the physician to examine for positive identification of the pinworms. Although pinworm infestations are usually self-limiting and not harmful to the patient, they produce some signs and symptoms of disease. These signs and symptoms include mild nausea or vomiting, loss of sleep, irritability, severe itching around the anus (important because the eggs can get on the hands during scratching and be ingested for re-infestation).

Figure 2-2. Pinworm.

d. **Ascaris lumbricoides** (pronounced AS-kar-is lum-bri-KOY-deez). Ascaris lumbricoides is usually referred to as the large intestinal roundworm (See Figure 2-3). The adult female intestinal roundworm ranges in size from 22 to 35cm, while the male is from 10 to 31cm. The adult worms typically live in the lumen of the small intestine. The worms subsist on the food present in the intestines and the cells of the host's intestinal mucosa. After the infective egg is ingested by the human, the egg hatches and the larva penetrate the wall of the small intestine. This larva then migrates through various parts of the body until it reaches the small intestine, where it remains until it dies. The spread of this parasite is made easier by poor sanitary conditions and poor hygiene. The eggs of Ascaris lumbricoides are frequently ingested by small children through hand to mouth contamination. Moist, loose soil provides a very favorable climate for the preservation of the eggs. Many infestations of this parasite go unnoticed by the host, since only a dozen or so worms are present. It is only when a worm is passed out in the stool or when a routine fecal examination is performed that the infection is diagnosed. Symptoms and signs associated with Ascaris lumbricoides infestation include cough, low-grade fever, pneumonia, intestinal obstruction (when many worms are present), and vomiting and abdominal pain (because of the movement of the worms).

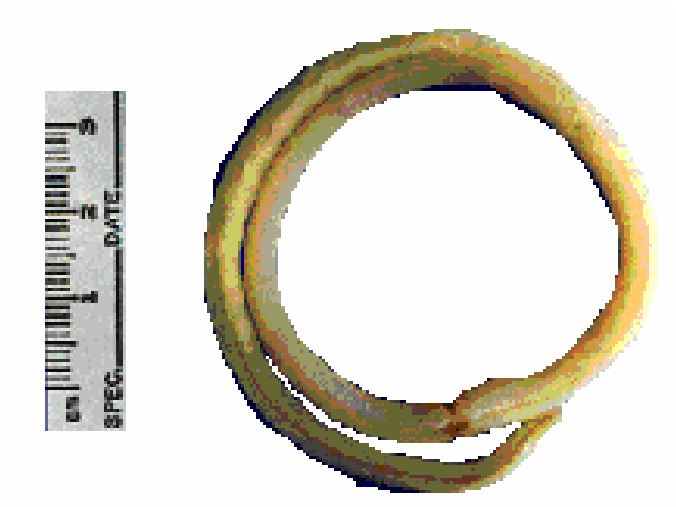


Figure 2-3. Giant roundworm.

e. **Ancylostoma duodenale** (pronounced AN-si-LOS-tuh-muh DEW-o-de-NAY-lee). Ancylostoma duodenale is commonly referred to as the Old World hookworm. This parasite is found primarily in Europe and South America. Adult hookworms are relatively small; males range from 5 to 11mm, and females range from 9 to 13mm. Humans are almost always hosts of this parasite. After the eggs are passed from the host, they hatch and become rhabditiform larvae. These larvae mature and derive some of their nutrition from organic matter in the soil. Later, they penetrate the skin of humans and travel through various locations in the body until the small intestine is reached. The presence of moist, warm soil is favorable for the spread of these parasites. The spread is also hastened by humans not wearing shoes (since the larvae penetrate through the skin of the feet). Signs and symptoms associated with Ancylostoma duodenale include the following.

(1) Severe itching at the point of penetration made by the larvae. This is called "ground itch."

(2) Mild pneumonia with sore throat, cough; and blood in the sputum. These signs and symptoms are caused by the migration of the larvae.

(3) Intestinal pain, enteritis, anemia, and weakness (caused by the blood sucking of the adult worms) when there are many worms present.

(4) Weight loss, slight anemia and slight loss of strength when there are a few worms present for a long time.

f. **Necator americanus** (pronounced Ne-KAY-tur ah-MERR-I-KAY-nus). Necator americanus is commonly referred to as the New World hookworm. This parasite is found in the United States, Asia, the South Pacific, and Africa. The life cycle for this organism is very similar to that of Ancylostoma duodenale (the Old World hookworm). Likewise, the signs and symptoms of infestation are the same as the Old World hookworm.

g. **Strongyloides stercoralis** (pronounced STRON-ji-LOY-dez STUR-ko-RAY-lis). Strongyloides stercoralis is commonly referred to as the threadworm. This parasite is found worldwide--especially in warm climates. Humans are the main hosts of this parasite. The parasitic female is from 2 to 3mm. There are free-living forms of this organism, depending on the environmental conditions (for example, moist, warm soil). Strongyloides stercoralis larvae invade the skin in much the same way as do the hookworms. Then the larvae migrate through the body until they reach the small intestine. The signs and symptoms associated with Strongyloides stercoralis include itchy, red patches on the skin at the site of penetration, bronchial pneumonia (because of movement of the larvae through the lungs), abdominal pain, diarrhea, constipation, vomiting and weight loss (when the parasites are in the intestines), and death (in some persons who are immunosuppressed due to heavy reinfection and migration of the larvae).

h. **Taenia saginata** (pronounced TEE-nee-uh sadj-I-NAT-tuh). This parasite is commonly referred to as the beef tapeworm. Taenia saginata is found in beef eating countries. The adults of this organism live in the small intestine. They are made up of segments (proglottids) and range from 2 to 10 meters in length. Infestation of this organism occurs in poorly cooked meat. In many cases, the tapeworm infestation goes unnoticed by the host until a proglottid is passed in the feces and observed by the host. With heavy infestations, weight loss, diarrhea, and abdominal pain can occur.

Section II. ANTIPARASITIC AGENTS

2-4. INTRODUCTION

With the potential for assignment throughout the world, soldiers are faced with the possibility of parasitic infestations. As a pharmacy specialist, you should be familiar with commonly used antiparasitic agents. Due to the constantly changing nature of the field, you should obtain a good up-to-date reference on the subject; this subcourse does not attempt to provide you with an all-inclusive and up-to-date listing of medications and their uses.

2-5. GENERAL COMMENTS PERTAINING TO ANTIPARASITE THERAPY

a. **Preventive Approach.** The preventive approach is the most economical and effective approach to treating parasitic infestations. Drugs are expensive, and there are adverse reactions and side effects associated with their use. Thus, the best approach to treating parasitic infestation is to prevent it from happening in the first place. How can one prevent parasitic infestation? Perhaps the key is knowledge of the life cycle of each parasite present in a particular area. Consider infestations by hookworms. Having bare feet in areas where hookworm infestations are prevalent certainly increases the likelihood of such an infestation. Soldiers should be informed of the importance of keeping on their boots.

b. **Parasitic Infestations.** Parasitic infestations occur throughout the world. When you enter an area, you should be informed of which parasites are most prevalent in that particular area. This knowledge will certainly have an impact on the drug products you stock in your pharmacy.

c. **Benefits/Txoic Effects.** The prescriber must weigh potential benefits of antiparasitic drug therapy against possible toxic effects produced by the drugs. Antiparasitic drugs, like other classes of medications, may have adverse effects. The person who prescribes a drug must determine if taking that drug will be more harmful than just leaving the patient as he/she is. The patient's age and state of health affect the prescribing of specific antiparasitic drugs.

d. **Administration of Anthelmintic Agents.** Oral anthelmintic agents are generally taken with water during or after meals. If pre or post-treatment purges are necessary (that is, to remove the worms from the gastrointestinal tract) in conjunction with a specific drug, magnesium sulfate or sodium phosphate may be used. The usual dose of these laxatives is 15 to 30 grams for an adult and 1 to 2 grams per 10 pounds of body weight for children. The laxative is to be dissolved in a glass of water. The laxatives may be taken in lemon juice (mixed with the water) to mask their intensely bitter taste. Magnesium sulfate must not be administered to persons with impaired renal function. Sodium phosphate may be contraindicated for patients with congestive heart failure. In general, anthelmintics are contraindicated for pregnant women and patients who have ulcers of the gastrointestinal tract.

2-6. SPECIFIC DRUGS USED IN THE TREATMENT OF AMEBIASIS INFESTATIONS

a. **Metronidazole (Flagyl®).** Metronidazole is used in the treatment of amebiasis, an infection of Entamoeba histolytica. Metronidazole is very effective in the treatment of acute intestinal amebiasis and amebic liver abscesses, symptomatic trichomoniasis, asymptomatic trichomonias is, and asymptomatic consort's T. vaginalis.

(1) Metronidazole is a chemically synthesized drug with trichomonacidal properties selected for obligatory anaerobic and facultative anaerobic organisms. Oral absorption of the drug is good, with both oral and IV administration, resulting in wide distribution to all body tissues, to include the CSF and saliva. The bulk of the drug remains unchanged, but active metabolites are formed. Sixty to eighty percent of the drug is eliminated in the urine, with a small portion excreted through the feces.

(2) Adverse reactions associated with this agent are not usually severe and include nausea, anorexia (loss of appetite), diarrhea, abdominal cramping, vertigo, and numbness of extremities. Convulsive seizures have also been reported. Patient taking metronidazole should be told to avoid alcohol, since alcohol and metronidazole may produce an Antabuse-type reaction (that is, produce nausea, vomiting, flushing, and abdominal cramps in the patient). Patients using this drug should be monitored for candidiasis super-infection. Metronidazole has been demonstrated to be a carcinogenic agent in some animals. Thus, as with all drugs, its use should be limited except in cases in which it is clearly indicated. In those cases, the prescriber should use the lowest effective dose. This product should not be prescribed to females who are in their first trimester of pregnancy because of the drug's effects on the fetus.

(3) In amebiasis, the adult dose of metronidazole (for acute amebic dysentery) is 750 milligrams by mouth three times daily for 5 to 10 days. In the treatment of amebic liver abscess, the dose of metronidazole is 500 to 750 milligrams taken orally three times daily for 5 to 10 days.

b. **Iodoquinol (Yodoxin®).** Iodoquinol is used in the treatment of amebiasis. This medication is especially destructive to amoeba in the intestinal tract. Occasional toxic effects associated with iodoquinol include rash, acne, nausea, and diarrhea. Patients who find the tablets too large to swallow whole should be instructed to crush the tablets and mix them with a small quantity of chocolate syrup or applesauce.

2-7. SPECIFIC DRUGS USED IN THE TREATMENT OF PARASITIC WORM INFESTATIONS

NOTE: When there is an infestation by two or more species of intestinal worms, the Ascaris infestation should always be treated first. Surgery may be required when heavy infestation with Ascaris lumbricoides produces intestinal perforation. When many worms are present, there can be partial or complete obstruction of the small intestine.

a. **Pyrantel Pamoate (Antiminth®).** Pyrantel pamoate is the drug of choice in the treatment of Ascaris lumbricoides (roundworm) and Enterobius vermicularis (pinworm) infestations. This drug acts to paralyze the worms. Once paralyzed, the worms are expelled from the gastrointestinal tract. Purges (that is, use of laxatives) are not used after the administration of this drug.

(1) This drug should be used with caution in patients who suffer from liver dysfunction. Adverse effects associated with this agent include anorexia, nausea, vomiting, abdominal cramps, and drowsiness.

(2) The caramel-flavored suspension contains 50 milligrams of pyrantel base per milliliter. For the treatment of pinworms and round worms, a single oral dose of 11 milligrams of pyrantel pamoate per kilogram of body weight is given. The maximum dose is 1 gram of pyrantel base. This corresponds to a dosage of 1 milliliter of pyrantel pamoate per 10 pounds of body weight (1 teaspoonful = 5 milliliters). Treatment may be given before or after meals. For pinworm infestations, the dose should be repeated in 2 weeks. For roundworm infestations, the dose should be repeated only if ova (eggs) are still found in the feces 2 weeks after the initial treatment.

b. **Mebendazole (Vermox®) Chewable Tablets.** Mebendazole is the broadest spectrum anthelmintic agent. It is used in the treatment of Trichuris trichiura (whipworm), Enterobius vermicularis (pinworm), Ascaris lumbricoides (roundworm), Ancylostoma duodenale (Old World hookworm), and Necator americanus (New World hookworm). Vermox® exerts its' anthelmintic effect by blocking glucose uptake by the susceptible worms, thereby depleting the worms' energy level until they cannot survive.

(1) This agent is contraindicated in pregnant women, and it should be used with caution with children under 2 years of age. Adverse reactions associated with this agent include transient abdominal pain and diarrhea. No pre or post-treatment purging is used with Vermox®. The 100 milligram chewable tablets should be chewed before they are swallowed.

(2) The dosage is the same for children and adults: 100 milligrams taken twice daily for three days for whipworms, hookworms, and roundworms. Then a stool sample should be examined for parasite ova in 2 to 3 weeks to determine if a second course of treatment is necessary. In a pinworm infestation, the dose is 100 milligrams taken one time only, this dose should be repeated in 2 weeks.

c. **Piperazine Citrate (Antepar®) Syrup/Tablets.** Piperazine citrate is used in the treatment of Ascaris lumbricoides (roundworm) and Enterobius vermicularis (pinworm). The drug produces a paralysis of the ascaris muscle with the resultant expulsion of the worm (while alive) through intestinal peristalsis one to three days after the initial treatment. The drug is relatively nontoxic to humans and usually produces no side effects if administered in anthelmintic doses. The ingestion of unusually large amounts of the drug may result in nausea, vomiting, diarrhea, abdominal pain, headaches, tumors, and blurring of vision. Excessively prolonged or repeated treatment should be avoided. The drug acts to paralyze the worms, and they are expelled (while alive) one to three days after the initial treatment. The safety of this drug, in regard to use during pregnancy, has not been established.

d. **Thiabendazole (Mintezol®).** Thiabendazole is a wide spectrum anthelmintic. It is the drug of choice in the treatment of Strongyloides stercoralis, (threadworm), Ascaris lumbricoides (roundworm), Necator americanus (New World hookworm), Ancylostoma duodenale (Old World hookworm), and Trichuris trichiura (whipworm) infestations. The mode of action of this drug is not fully understood at this time, but experimental studies have shown that the presence of this drug inhibits the normal development of eggs. As in the case of other drugs, the use of this agent may cause some adverse reactions such as nausea, vomiting, dizziness, and anorexia. In some cases, the use of thiabendazole has caused erythema multiform, which can be fatal to children. Thiabendazole should be used with caution in patients with hepatic or renal dysfunction. Patients should be advised against performing tasks requiring mental and/or physical alertness on days when the drug is taken. Also, there is some indication that prolonged use of this drug may stimulate the migration of roundworms. The tablets should be chewed before they are swallowed. The safety of thiabendazole has not been established for pregnant women and women who are breast-feeding.

e. **Pyrvinium Pamoate (Povan®) Tablets/Oral Suspension.** Pyrvinium pamoate is the salt of a dye. Pyrvinium pamoate is used as an alternative drug in the treatment of Enterobius vermicularis (pinworm) infestations. This drug is not appreciably absorbed from the gastrointestinal tract.

(1) Pinworm infection can easily pass from person to person by the transfer of eggs through direct contact, the handling of contaminated objects, and the breathing in of airborne eggs. Therefore, if an infection is detected in a family member or institutionalized group, treatment of all members should be considered for complete parasite eradication.

(2) To avoid undue concern and to help avoid accidental staining, patients and parents should be advised of the staining properties of pyrvinium. Tablets should be swallowed whole to avoid staining of teeth. If the suspension is spilled, it will stain most materials. The agent will also color the stool a bright red, which is not harmful to the patient. If emesis (vomiting) occurs, the vomitus will probably be colored red and will stain most materials.

(3) Since the gastrointestinal tract of adults does not appreciably increase in size with increased weight gain, the dosage for adults need not exceed that recommended for a patient weighting 154 pounds. A single dose of 7 teaspoonfuls of the oral suspension should be adequate for patients who weigh more than 154 pounds.

(4) Adverse reactions associated with this drug include nausea, vomiting, cramping, and diarrhea.

f. **Paromomycin (Humatin®).** Paromycin is used as an alternative drug of choice (not an approved Food and Drug Administration indication) for tapeworm (cestodes) infestation. This drug is also used in the treatment of amebiasis. Paromycin is a broad-spectrum antibiotic that is poorly absorbed from the gastrointestinal tract. Adverse effects associated with this agent include abdominal pain, diarrhea, nausea, and vomiting. This agent has the potential for causing nephrotoxicity, ototoxicity, and central nervous system toxicity. It should be used with caution by patients who have ulcerative lesions of the bowel to avoid renal toxicity through inadvertent absorption. Paromycin should not be used by persons who have intestinal obstructions.

g. **Niclosamide (Niclocide®).** Niclosamide is the drug of choice in the treatment of tapeworms. The scoleces and proximal segments of the cestode are rapidly killed on contact with this agent. Concomitant use of a laxative is not necessary except in the treatment of Taenia saginata (beef tapeworm) infections. It should be used with extreme caution in children under the age of 2 years due to lack of experience with the drug in this age group. The tablets should be crushed or chewed before being swallowed. Some patients may experience mild nausea and vomiting.

h. **Emetine hydrochloride.** Emetine hydrochloride is the drug used in the treatment of intestinal and extraintestinal amebiasis. Because of its toxicity, patients should be hospitalized during treatment with emetine. Adverse effects with the use of this drug include precordial pain, tachycardia and other arrhythmias, congestive heart failure, dyspnea, and hypotension. Nausea, vomiting, dizziness, headache, and skeletal muscle weakness may also occur. This drug should not be used in patients with a history of cardiac or renal disease or in pregnant women. It should not be used by young children unless alternative drugs have not been effective.

Continue with Exercises

EXERCISES, LESSON 2

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. A purge is:

   a. The administration of a cathartic to a patient in order to remove parasites from the patient's intestines after the patient has taken an anthelmintic drug.

   b. A chemical substance used to eradicate or reduce in numbers helminthic parasites in the intestinal tract or tissue.

   c. A drug used to paralyze intestinal parasites so they can be removed from the intestinal tract.

   d. The surgical removals of large numbers of intestinal parasites from a patient after the worms have obstructed the patient's small intestine.

2. Enterobius vermicularis is commonly referred to as the:

   a. Old World hookworm.

   b. Roundworm.

   c. Tapeworm.

   d. Pinworm.

3. Ascaris lumbricoides is commonly referred to as the:

   a. Pinworm.

   b. Large intestinal roundworm.

   c. Tapeworm.

4. Strongyloides stercoralis is commonly referred to as the:

   a. Old World hookworm.

   b. New World hookworm.

   c. Threadworm.

   d. Pinworm.

5. The trade name of iodoquinol is:

   a. Flagyl®.

   b. Vermox®.

   c. Mintezol®.

   d. Yodoxin®.

6. Which of the following is the drug of choice in the treatment of Strongyloides stercoralis infestations?

   a. Thiabendazole.

   b. Pyrvinium pamoate.

   c. Paromycin.

   d. Pyrantel pamoate.

7. Which of the following is the trade name of paromomycin?

   a. Antiminth®.

   b. Humatin®.

   c. Povan®.

   d. Vermox®.

8. Persons taking metronidazole (Flagyl®) should be cautioned:

    a. That they will become drowsy after taking the drug.

    b. That the stool will be colored red because of taking the medication.

    c. That the drug can cause nephrotoxicity, ototoxicity, and central nervous system toxicity.

    d. Not to drink alcohol while taking the drug.

9. Adverse reactions associated with the use of Antepar include:

    a. Anorexia and dizziness.

    b. Ulcerative lesions of the bowel and renal toxicity.

    c. Nausea, vomiting, and abdominal pain.

    d. Acne and rash.

10. Yodoxin® is used in the treatment of:

    a. Amebiasis.

    b. Ascaris lumbricoides infestations.

    c. Enterobius vermicularis infestations.

    d. Tapeworm (cestodes) infestation.

11. Paromomycin (Humatin®) is used as an alternative drug of choice (not an FDA approved indication) for the treatment of:

    a. Strongyloides stercoralis infestation.

    b. Trichuris trichiura (whipworm) infestations.

    c. Tapeworm (cestodes) infestation.

    d. Enterobius vermicularis (pinworm) infestations.

12. Which of the following is the broadest spectrum anthelmintic agent?

    a. Piperazine citrate.

    b. Mebendazole.

    c. Pyrantel pamoate.

    d. Iodoquinol.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 2

1. a (para 2-2f)
2. d (para 2-3c)
3. b (para 2-3d)
4. c (para 2-3g)
5. d (para 2-6b)
6. a (para 2-7d)
7. b (para 2-7f)
8. d (para 2-6a)
9. c (para 2-7c)
10. a (para 2-6b)
11. c (para 2-7f)
12. b (para 2-7b)

End of Lesson 2

LESSON ASSIGNMENT

LESSON 3	Antibiotics and Sulfonamides.
TEXT ASSIGNMENT	Paragraphs 3-1 through 3-17.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

3-1. Given the trade name of an antibiotic or sulfonamide agent and a list of generic names, select the generic name that corresponds to the trade name.

3-1. Given an antibiotic or sulfonamide agent and a list of side effects/toxicities, select the side effects/toxicities associated with that agent.

3-3. Given a generation of cephalosporins and a list of spectrums of activity, select the spectrum of activity associated with that generation of cephalosporins.

3-4. Given a caution/warning associated with antibiotics or sulfonamides and a list of antibiotics or sulfonamide agents, select the agent associated with that caution/warning.

3-5. Given a specific organism and a list of classifications of penicillins, select the penicillin that would be effective in treating an infection caused by that organism.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 3

ANTIBIOTICS AND SULFONAMIDES

3-1. INTRODUCTION

a. Infection is the invasion of the body by a pathogenic organism, the tissue's reaction to the organism, or the tissue's reaction to a toxin produced by the organism. An infection occurs when the organism exerts its effect upon the cells or when host resistance is reduced. Resistance can be reduced if the normal immune process is compromised or changes occur in the normal makeup of organisms (flora) which give a harmful organism the opportunity to thrive.

b. The human body has numerous built in barriers against infections. Mechanical barriers include the skin and mucous membranes. Acids in the stomach form a chemical barrier that kills bacteria found there. A third natural barrier is the normal flora existing in the body. There are normally many different types of organisms growing on the skin and in body cavities all competing with each other for nutrients and inhibiting the overgrowth of the other organisms. When something happens to disturb this natural balance (as when an antibiotic kills a large number of bacteria), the remaining organisms can then flourish and cause a problem. A good example of this is the overgrowth of yeast, which can occur in the presence of long term antibiotic therapy. The final barrier is the body's inflammatory process, which is initiated when there is tissue damage. Mast cells rupture and release histamine, while other mediators cause vasodilatation and in creased capillary permeability. This allows better access to the inflamed area by infection fighting cells.

3-2. ANTI-INFECTIVE AGENTS

An anti-infective or antimicrobial agent is a drug that is used in the treatment or prevention of infections. These agents are also sometimes referred to as chemotherapeutic agents, although this term is also commonly applied to drugs used to treat cancer and really applies to any chemical (drug) used for medical therapy. Antibiotics and sulfonamides are two examples of these agents. The group of organisms against which an agent is effective is called its spectrum. Broad-spectrum antibiotics are effective against a wide range of microorganisms, usually specific microorganisms in both gram positive and positive organisms only.

a. Bactericidal drugs are those drugs that <u>kill</u> pathogens. This can be accomplished by one of three methods:

(1) The drug disrupts cell wall synthesis of bacteria.

(2) The drug acts directly on cell membranes to increase permeability, leading to leakage of the bacteria's intracellular contents.

(3) The drug affects the bacterial cell's DNA, causing production of abnormal protein.

b. A drug or antibiotic that inhibits the reproduction of pathogens is called bacteriostatic. These drugs slow down the growth of an infection and give the natural defenses of the body a better opportunity to combat the infection on their own. They work in two ways. They may affect the function of the bacterial ribosomes, resulting in a reversible disruption of protein synthesis or they may block steps in the bacteria's metabolic pathways that are essential to the life of the microorganisms.

3-3. BACTERIAL RESISTANCE TO ANTI-INFECTIVE AGENTS

Bacteria are constantly becoming resistant to anti-infective agents. This is one of the major reasons that new antibiotics are continually appearing on the market. As bacteria encounter a drug, they may begin forming new enzymes that destroy the drug more rapidly, making the drug ineffective. Such an enzyme is beta lactamase that deactivates such agents as penicillins and cephalosporins. Phosphorylating and acetylating enzymes, which change the structure of a drug, may render gram-negative bacteria resistant to certain antibiotics. Additionally, when an agent is used over an extended period, changes in the bacterial cell wall may make it less permeable to the drug. If the drug blocks one of the steps in the bacteria's metabolic pathway, the bacteria may develop an alternate pathway which by-passes the block, just as a road detour can bypass an area where a road is blocked. There are also numerous other ways in which microorganisms can develop resistance to antibiotics. Over the past several decades, early abuse of antibiotics when they were not really needed and inappropriate therapy have contributed to the development of resistance. The prudent use of antibiotic therapy and the appropriate selection of agent and type of therapy can minimize the development of resistant strains of bacteria.

3-4. ANTIBIOTIC SELECTION

When selecting an anti-infective agent, it would seem that the easiest thing to do would be to use the antibiotic with the broadest spectrum. In fact, the best approach in therapy is to select the agent that is the most effective against the specific bacteria causing the infection. In order to do this microscopic examination, staining, or culturing in the laboratory can identify the organism. When an organism is cultured, it is also possible to determine its sensitivity to different antibiotics, as well as the antibiotic concentration required for effectiveness, the minimum inhibitory concentration (MIC). In this way, the most effective agent can be selected. Because a culture and sensitivity (C&S) takes several days to perform, the physician will usually evaluate several factors, such as patient condition, specific symptoms, and other similar cases which have been seen in ma king an initial antibiotic selection. When the C&S is available, the initial anti-biotic may be changed to one that is more effective, or if the patient's response has been satisfactory, the original selection may be continued.

3-5. ANTIBIOTIC COMBINATION

There are many instances when combining two or more antibiotics is necessary or desirable in treating an infection or disease. This may be the case when there is a mixed infection, in which there may be several organisms, or when there is a severe or life threatening infection of unknown origin. By combining several agents, they can sometimes be made more effective than either agent alone (synergy), thus allowing lower doses and reducing complications of therapy. With certain organisms, the use of combination therapy is necessary to prevent rapid resistance to the drug that is used.

3-6. CHEMOPROPHYLAXIS

Chemoprophylaxis is the use of antibiotics to prevent infection in a healthy individual or to prevent infection by other organisms (called superinfection) in an individual already being treated for an infection. This generally involves giving low doses of a drug on an infrequent schedule. For example, individuals who have had rheumatic fever as children may take a sulfonamide once a day (instead of the four times daily needed for treating an infection) to prevent the development of bacterial endocarditis, a life-threatening infection involving the heart.

3-7. SUPERINFECTIONS

Superinfections may occur during the use of anti-infective therapy. This is simply the overgrowth of nonsusceptible normal body flora. There is always an alteration of body flora, particularly that found in the GIjettie@cyberback.com , urinary, and respiratory tract during antibiotic therapy. Usually, the organism that tends to overgrow is Pseudomonas, Candida, fungi, or beta-lactamase producing staphylococci. Superinfection is most noticeable when broad-spectrum antibiotics have been administered over a period of 14 days or more.

3-8. PENICILLIN GROUPS

a. **Natural Penicillin.**

(1) Natural penicillins are derived from certain species of molds and other fungi. They produce their effects by inhibiting biosynthesis of cell wall mucopeptides. All classes of penicillin are bactericidal.

(2) Oral absorption of natural penicillin is incomplete and variable, except for the newer penicillin VK products. Oral absorption becomes more predictable if the penicillin is taken on an empty stomach, 1 hour before or 2 hours after meals. IV and IM routes produce transient, high-blood levels of the antibiotic. Penicillin is widely distributed to all tissues, especially soft tissues. However, it is not distributed to ocular, skeletal and cardiac muscle and to cerebrospinal fluid unless inflammation is present.

(3) Natural penicillins are not affected by the metabolic process and are excreted unchanged. Excretion is very rapid via the kidneys but can be retarded by the concurrent administration of probenecid. Combining penicillin G with procaine or benzathine may also retard excretion. This increases the amount of penicillin available in the body, prolonging the action and increasing the effectiveness.

(4) Dosage of the natural penicillins depends on the dosage form and the type and severity of the infection being treated. Parenteral doses are measured in units, with one unit equal to 0.6 mg of standard penicillin, USP.

(5) The natural penicillins are narrow spectrum antibiotics primarily effective against gram-positive and a few gram-negative bacteria. They are the first drugs of choice in the treatment of infection caused by gram-positive cocci and bacilli, gram-negative bacilli bacteroides, cocci, and spirochetes.

(6) The most common adverse reaction to these drugs is hypersensitivity. The degradation product, penicillenic acid, probably causes this. The most common manifestation is skin rash, with the most lethal reaction being anaphylactic shock. This reaction may vary from a mild fever, rash, or leukopenia to severe arthralgia or arthritis. Oral preparations may cause nausea and vomiting, epigastric distress, diarrhea, and black hairy tongue. Superinfections may occur but are rare.

(7) The use of natural penicillin is contraindicated in patients with penicillin allergy, which should be used with caution in patients with histories of other allergies. When administered, especially parenterally, steps should be taken to ensure that agents are available to manage hyper-sensitive reactions and to monitor the patient at least 30 minute s after he receives a parenteral injection. The usual course of therapy is 7-10 days, and the patient should be instructed to complete it.

(8) The natural penicillins are found in the following preparations:

(a) K+ or Na+ penicillin G (Penicillin G®).

(b) Procaine penicillin G (Wycillin®, Crysticillin®).

(c) Benzathine penicillin G (Bicillin LA®, Permapen®).

(d) Penicillin V potassium (V-Cillin®, Pen-Vee K®).

b. **Penicillinase Resistant Penicillins.**

(1) Penicillinase is an enzyme produced by certain bacteria, which converts penicillin to an inactive product and thus increases resistance to the drug. Drugs in this group are structurally resistant to beta-lactamase activity, interfere with transpeptidases of the cell, and are bactericidal.

(2) These penicillins are all excreted via the kidneys, with the exception of nafcillin, which is excreted via the biliary canal.

(3) This class is to be used when staphylococcal beta-lactamase infection is known or suspected. The organism in this case is S. aureus. Seventy percent of all community acquired staphylococcal infections are beta lactamase producing.

(4) Adverse reactions, cautions, and warnings for these drugs are the same as those for the natural penicillins. Some hepatotoxicity can be produced as noted by transient high levels of SGOT, SGPT, and LDH, especially with the use of oxacillin.

(5) These penicillins are available in the following preparations:

(a) Methicillin Na (Staphcillin®).

(b) Nafcillin Na (Unipen®).

(c) Oxacillin Na (Prostaphlin®).

(d) Cloxacillin Na (Tegopen®).

(e) Dicloxacillin Na (Dynapen®).

c. **Broad-Spectrum Penicillins.**

(1) Drugs belonging to this class are natural penicillins that have been chemically modified. They are very similar to the natural penicillins in their method of action, metabolism and excretion, reaction, cautions, and warnings.

(2) These drugs are employed against the same microbes as the natural penicillins, but also have an increased chemical activity against Proteus mirabilis, Haemophilus influenzae, and E. coli.

(3) Resistance to these drugs is acquired by the gram-negative organisms. Additionally, the drugs are inactivated by beta-lactamase.

(4) These drugs are used for soft tissue infections, such as the respiratory, urinary, and gastrointestinal tract as well as otitis media infections. Some authorities consider them the drug of first choice in the treatment of uncomplicated gonorrhea.

(5) Broad-spectrum penicillins are ampicillin, which is indicated for both parenteral and oral use, and amoxicillin, which is for oral use only.

d. **Broad Spectrum Antipseudomonal Penicillins.**

(1) These drugs are widely distributed in most body fluids as with all penicillins. Carbenicillin is distributed into the non-inflamed CSF (cerebrospinal fluid), which is not typical of most antibiotics.

(2) The spectrum of activity of these drugs has been increased to combat Pseudomonas aeruginosa and some strains of Proteus that are resistant to ampicillin.

(3) Patients taking large doses of these antibiotics must have their serum sodium levels closely monitored as these drugs contain excessive amounts of sodium. Resistance to these drugs is acquired very quickly if they are used alone. High serum levels potentiate neurotoxicity manifested by lethargy, neuromuscular irritability, and seizures.

(4) In this group of penicillins, the following preparations are found:

(a) Carbenicillin disodium (Geopen®, Pyopen®).

(b) Carbenicillin indanyl sodium (Geocillin®).

(c) Ticarcillin disodium (Ticar®).

(d) Azlocillin Sodium (Azlin®).

e. **Broad-Spectrum Antipseudomonal Penicillin with Activity Against Klebsiella.**

(1) This penicillin has properties similar to those of the natural penicillins. They possess the same bactericidal activity as carbenicillin; in addition, they are effective against Klebsiella. Some agents are more active against Pseudomonas than carbenicillin.

(2) These drugs can be found as mezlocillin (Mezlin®), or piperacillin (Pipracil®) which is the most active of all the penicillins against Pseudomonas.

3-9. THE CEPHALOSPORINS

a. These drugs have their origin in Cephalosporium acremonium, a fungus. This fungus contains three antibiotics of which cephalosporin C has the most promise for chemical modification. These modifications have proliferated to include three generations currently on the market and a fourth being prepared for marketing.

b. The action of the cephalosporins is similar to the penicillins, and they are bactericidal.

c. These agents are widely distributed to most body tissues and fluids with maximum concentrations in the liver and kidneys. Penetration of the CSF is accomplished only by moxalactam that penetrates with or without inflamed meninges. Therapeutic blood levels are reached in bone with the use of cephradine, cefamandole, and cefazolin. Cefazolin levels are even higher in inflamed bone tissue.

d. Metabolism does occur with some agents, but their metabolic byproducts show less antibacterial activity. The kidneys through glomerular filtration and tibular secretion excrete all of the cephalosporins.

e. Because of the many products available, it is best to check the appropriate literature for dosage information. Depending on the agent's characteristics and route of administration, the dose may vary from 500mg to 12g per day.

f. First generation agents.

(1) The prototype of first generation cephalosporins is cephalothin (Keflin®). These agents are effective against gram-positive and a large number of gram negative organisms. Gram-positive bacteria include Group A strep pyrogenes, beta-lactamase producing and non-producing staph aureus, clostridium perfringens, and many other streptococcal infections. Examples of gram-negative include N. gonorrhea, Salmonella, most Shigella and Proteus, 75 percent of E. coli, 50 percent of H. influenzae, and all strains of Klesbiella.

(2) Hypersensitivity is the most common adverse reaction of these agents, especially in patients with demonstrated immediate allergic reaction to penicillin. A rash may develop after several days of therapy and may or may not be accompanied by fever or eosinophilia. High doses of first generation agents will cause a positive Coombs' reaction, but hemolysis seldom occurs. High doses may also cause nephrotoxicity, especially in elderly patients. Administering these agents intravenously can cause thrombophlebitis, and IM injections are painful.

(3) With first generation cephalosporin therapy, all patients should be monitored for superinfection, and elderly patients should have their renal functions monitored.

(4) The first generation cephalosporin preparations are:

(a) Cephalothin (Keflin®).

(b) Cephalexin (Keflex®).

(c) Cefadroxil (Duricef®).

(d) Cephradine (Velosef®, Anspor®).

(e) Cephapirin (Cefadyl®).

(f) Cefazolin (Ancef®, Kefzol®).

g. Second generation agents.

(1) These agents are similar to first generation agents; in addition, they are active against Haemophilus influenzae, including ampicillin resistant strains. They are also beta-lactamase resistant. Some agents are more active against gram-negative bacilli, especially indole positive Proteus and anaerobes.

(2) Second generation cephalosporin agents cause adverse reactions similar to first generation agents and require the same cautions and warnings.

(3) Examples of these agents are:

(a) Cefaclor (Ceclor®).

(b) Cefamandole (Mandol®).

(c) Cefoxitin (Mefoxin®).

h. Third generation agents.

(1) These agents are parenteral antipseudomonal cephalosporins with expanded activity against gram-negative organisms, but less activity against gram-positive organisms than the previous generation.

(2) Because of its good CSF penetration, moxalactam may be the initial drug to use when a gram-negative bacilli is stained from a meningeal infection. However, this agent is reported to cause hypoprothrombinemia. and it should be administered concurrently with vitamin K.

(3) These agents cause similar adverse reactions and require the same cautions and warnings as previous generations.

(4) Some examples of third generation cephalosporin agents are:

(a) Cefoperazone (Cefobid®).

(b) Cefotaxime (Claforan®).

(c) Moxalactam (Moxam®).

3-10. ERYTHROMYCIN

a. Erythromycin is a product of the fungus Streptomycesery threus, which was first found in a soil sample collected in the Philippine Islands. This agent inhibits protein synthesis to exert bacteriostatic activity.

b. Erythromycin is acid labile unless it is formulated in an enteric coated form or is combined with a salt such as stearate or ethylsuccinate. It is distributed to most body tissue and is prominent in prostatic fluid. There is minimal concentration of this agent in the CSF unless there is meningitis.

c. The clinical spectrum of this agent is similar to penicillin G, and it is the drug of choice in the treatment of mycoplasma pneumonia and Legionnaire's disease. It is a useful substitute for penicillin in people who are hypersensitive to penicillin.

d. Adverse reactions to erythromycin are similar to the penicillins except that estolate salt has been known to cause cholestatic hepatitis. Therefore, it should not be used in patients with pre-existing liver disease. Large oral doses of erythromycin can cause epigastric distress.

e. As an antibiotic agent, erythromycin can be found in the following preparations: Erythromycin base (EMycin®), Erythromycin estolate (Ilosone®), Erythromycin stearate (Erythrocin®), and Erythromycin ethylsuccinate (E.E.S. ®).

3-11. CLINDAMYCIN (CLEOCIN®)

a. Clindamycin is derived from the actinomycete Streptomyces lincolnensis. A bacteriostatic agent suppresses protein synthesis.

b. When taken orally, absorption of clindamycin is rapid and almost complete. It is widely distributed to body tissues with the exception of the CSF (cerebrospinal fluid).

c. Enzymes in the liver accomplish metabolism of the agent. The metabolites are excreted through the urine and bile.

d. Clindamycin is indicated in the treatment of serious infections caused by anaerobic bacteria. It is the drug of choice for use against Bacteroides fragilis.

e. Adverse reactions noted with the use of clindamycin include abdominal pain, esophagitis, nausea, vomiting, and diarrhea. Colitis, which can be fatal, is a serious reaction to this agent. Consequently, other less toxic agents, such as erythromycin or penicillin, should be used if possible. If significant diarrhea or colitis appears while the patient is using clindamycin, its use should be discontinued. This colitis can then be treated with the agent vancomycin.

3-12. THE AMINOGLYCOSIDES

a. These agents are a result of a systematic search to find an antibiotic that was effective against gram negative bacteria. During this research, a strain of actinomycetes, Streptomyces griseus, was isolated. It produced a potent antimicrobial leading to the discovery of streptomycin. These agents are bactericidal in nature; their MOA is to inhibit protein synthesis.

b. The body normally cannot absorb these agents when administered orally. They must be administered by either IM or IV routes. They are widely distributed in body fluids, except the CSF and the eye. They are found mainly in extracellular fluid.

c. The aminoglycosides are excreted unchanged by glomerular filtration. Elimination is dependent almost exclusively on renal function. The incidence of nephrotoxicity and ototoxicity is directly related to the concentration to which aminoglycosides accumulates in the serum.

d. The initial dose for these agents depends, of course, on the agent used. After the initial dose has been administered, it is best to use serum peak and trough levels to estimate subsequent doses. Consistent peak serum levels seem to make the patient more prone to ototoxicity. Elevated trough levels lead to nephrotoxicity.

e. Streptomycin is occasionally used in combination with isoniazid in the treatment of tuberculosis. Neomycin and kanamycin are seldom used parenterally. When used in their oral form, they suppress the flora of the GI tract prior to surgery. Occasionally, kanamycin is used parenterally by pediatricians for gram negative bacteria; it is not effective against Pseudomonas. Gentamicin, tobramycin, and amikacin, in combination with carbenicillin, are used primarily in serious gram-negative infections, especially Pseudomonas aeruginosa. Amikacin is the most effective aminoglycoside against gentamicin resistant strains and is generally reserved for these cases.

f. Ototoxicity, which is some cases may be irreversible, occurs more frequently with the use of streptomycin, neomycin, and kanamycin. This reaction causes cochlear and vestibular damage leading to hearing loss, vertigo, ataxia, and loss of balance.

g. The incidence of nephrotoxicity, which is irreversible, occurs about 2-10 percent of the time and is more prevalent with the use of neomycin than any of the other agents. The factors that contribute to the incidence are: dose of the agent used, pre-existing renal damage, and contracted intravascular volume caused by the use of diuretics:

h. Prolonged high doses of any of the aminoglycosides may exert a curare-like effect on various body systems.

i. When any of the aminoglycosides are used, concomitant use with general anesthetics or neuromuscular blocking agents should be monitored because of recognized drug interactions. Additionally, the use of rapidly acting diuretics should be avoided, as ototoxicity and nephrotoxicity can be potentiated with their use. Renal functions should be monitored continuously when these agents are used.

j. Spectinomycin (Trobicin®) has an action similar to that of the aminoglycosides but without bactericidal action. It is used in the treatment of gonorrhea in patients that are hypersensitive to penicillin and cannot tolerate one of the tetracyclines. It is also used in the treatment of penicillinase producing Neisseria gonorrhea (PPNG). Spectinomycin is usually given in a single IM dose, the strength of which is dependent on unknown resistance factors. There are very few adverse reactions of any significance associated with the use of this agent. However, it should not be used in the treatment of syphilis, and its safety in pregnant women has not been established.

3-13. TETRACYCLINES

a. These drugs originate from strains of Streptomyces containing broth that is fermented in deep tanks. Most of these agents are the result of chemical modifications of the broth by product. All of them are bacteriostatic. Their MOA is to inhibit protein synthesis in the microorganism.

b. If administered orally, absorption of these agents occurs primarily in the stomach and the upper portion of the small intestine. Administration intravenously results in wide distribution of the agent throughout the body, with penetration of the CSF.

c. Excretion of these agents occurs through either the urinary or the biliary tract, with the urinary tract as the primary route. Doxycycline is excreted almost exclusively through the feces. Minocycline appears to be the only agent that is metabolized, whereas the others are excreted unchanged.

d. The tetracyclines are true broad-spectrum antibiotics effective against gram positive and gram-negative bacteria. Agents in this group are the drugs of choice when treating Mycoplasma pneumoniae, chlamydia, cholera, and Rocky Mountain spotted fever. They are also used in the treatment of gonorrhea in patients hypersensitive to penicillin and in high doses in the treatment of syphilis in patients hypersensitive to penicillin.

e. Gastrointestinal reactions are common with the use of tetracyclines. Some of these conditions are epigastric distress, nausea, vomiting, diarrhea, and general abdominal discomfort. Hepatic and renal toxicity, photosensitivity, permanent discoloration of the teeth in pediatric patients or fetus, CNS vestibular disturbances, and other local irritations are additional adverse reactions associated with the use of these agents.

f. Tetracyclines should not be used in children during tooth development, which occurs in the last half of pregnancy, infancy, and through childhood up to 8 years of age. The tetracyclines can cross the placenta and have direct toxic effects on the bones of the developing fetus. They also appear in the milk of lactating mothers. Antacids, milk, dairy products, iron, or foods containing aluminum, calcium, or magnesium should be avoided when these agents are taken orally. The tetracyclines should never be used with the penicillins.

g. Tetracyclines appear in the following preparations:

(1) Tetracycline HCl (Achromycin®, Tetracyn®, Sumycin®)

(2) Doxycycline (Vibramycin®)

(3) Minocycline (Minocin®)

3-14. CHLORAMPHENICOL (CHLOROMYCETIN®).

a. This drug is produced by Streptomyces venezuelae, an organism first isolated in 1947 from a soil sample collected in Venezuela. It is bacteriostatic for most organisms and works by inhibiting protein synthesis.

b. Chloramphenicol is absorbed well by the body when it is administered orally. When it is administered IM, its absorption is questionable; therefore parenteral doses should be given IV. Distribution is generally good in all body fluids with concentration in the liver and kidneys. Therapeutic levels are achieved in the CSF without inflammation. Measurable levels can be detected in aqueous, vitreous humors, and bile.

c. During the metabolic process, most of the drug unites with glucuronic acid, and the free drug and metabolites are excreted through the urine.

d. Chloramphenicol is used in the treatment of serious infections such as meningitis and is the drug of choice in the treatment of typhoid fever.

e. Some of the adverse reactions associated with the use of this drug include aplastic anemia (which is irreversible and fatal when it occurs), gastrointestinal tract discomfort, and “gray baby syndrome” in infants. This is an absence or deficiency of certain enzymes during early neonatal life that prolongs the half-life of certain drugs and increases the half life of others, thus increasing the risk of toxicity. For example, immaturity of hepatic glucuronyl transferase activity in neonates diminishes conjugation (metabolism) of chloramphenicol to the inactive form, causing cardiovascular collapse and death.

f. To avoid these reactions, baseline blood studies, prior to therapy and periodic checks every 2 days during therapy, is recommended. The drug should not be used in pregnant patients.

3-15. METRONIDAZOLE

a. Metronidazole is a chemically synthesized drug with trichomonacidal properties selective for obligatory and facultative anaerobic organisms.

b. Oral absorption of the drug is good with both oral and IV administration resulting in wide distribution to all body tissues to include the CSF and saliva.

c. The bulk of the drug remains unchanged, but active metabolites are formed. Sixty to 80 percent of the drug is eliminated in the urine with a small portion excreted through the feces.

d. Adverse reactions associated with this agent are not usually severe and include nausea, anorexia, diarrhea, abdominal cramping, vertigo, and numbness of the extremities. Convulsive seizures have been reported with the use of this drug.

e. Patients using this drug should be monitored for candidiasis superinfection. It should not be used in the first trimester of pregnancy or in breast-feeding mothers because of its carcinogenic potential. Patients should avoid alcoholic beverages while taking the drug.

f. Examples of metronidazole preparations are:

(1) Flagyl® IV.

(2) Flagyl® IV RTU.

(3) Flagyl® 250 mg.

3-16. TOPICAL ANTI-INFECTIVES

a. These agents are used to help prevent or treat infection in minor cuts, burns, and abrasions. This use occasionally allows the overgrowth of nonsusceptible organisms, including fungi. Ideally, the topical application of these agents used systemically should be avoided because of sensitization. Systemic antibiotics are preferred in deeper, chronic infections.

b. Examples of these agents are:

(1) Bacitracin Ointment.

(2) Bacitracin-Neomycin Ointment.

(3) Povidone-Iodine (Betadine®) Ointment.

3-17. THE SULFONAMIDES

a. The compound p aminobenzenesulfonamide, now known as sulfanilamide, was first synthesized in 1908, but it was not until many years later that its therapeutic value was known. In 1932, a red dye was prepared; it was later reported to have remarkable curative effects and was named Prontosil®. It was found that the bacterial property of the drug rested in the p aminobenzenesulfonamide portion of the molecule. In 1937, sulfapyridine, which was the first sulfonamide used with great success in treating pneumonia, was synthesized. Since that time, over 3300 sulfonamides have been prepared, but only a few have been accepted for medical use.

b. The sulfonamides possess a wide antimicrobial spectrum, which include both gram-positive and gram-negative organisms. These agents compete with p-aminobenzoic acid and prevent its normal cellular utilization, particularly its incorporation into folic acid.

c. Most of the sulfonamides are absorbed from the gastrointestinal tract and distributed throughout the body. They should be taken with large amounts of water.

d. They are metabolized by enzymes in the liver, resulting in a product with no antimicrobial activity. Both the free drug and its metabolites are excreted through the kidneys.

e. Dosage of these agents is varied. Oral administration is preferred since parenteral forms are quite irritating to tissue. Short acting sulfonamides are usually given at 4 to 5 hour intervals and an initial loading dose is usually recommended. Longer acting agents are usually given every 8 to 12 hours.

f. There is a low incidence of adverse reactions with these agents. Some of the more common are large varieties of skin rashes, serum sickness, drug fever, acute disorders of the hematopoietic system, and disturbances of the urinary tract.

g. Sulfonamides should be used with caution in the presence of renal and hepatic dysfunction. Periodic complete blood counts should be done to monitor the patient for any possible blood disorders. They should be used cautiously in the presence of other highly protein binding drugs and in patients that are glucose-6-phosphate dehydrogenase (G-6-PD) deficient. Patients should maintain adequate fluid intake to prevent cystalluria in less soluble compounds.

h. Sulfonamide preparations.

(1) Sulfisoxazole (Gantrisin®)

(a) This is a short acting compound with good solubility and is the first drug of choice for urinary tract infections. The initial dose ranges from 2 to 4 grams, with maintenance dose ranging from 4 to 8g daily.

(b) Sulfisoxazole is indicated as a prophylactic for rheumatic fever in patients allergic to penicillin.

(c) Other sulfonamide preparations include:

1 Sulfamethizole (Thiosulfil Forte®).

2 Sulfadiazine (Microsulfan®).

3 Sulfamethoxazole (Gantanol®).

(2) Bactrim®, Septra®.

(a) These agents are derived from a combination of trimethoprim and sulfamethoxazole.

(b) There are many uses for this product. Its major use is in the treatment of chronic urinary tract infections. It is also indicated in the treatment of acute otitis media in children and the treatment of shigellosis and resulting enteritis if it is resistant to ampicillin and tetracycline.

(c) The dose for this drug depends on its strength and how it is to be utilized.

(3) Sodium sulfacetamide (Sulamyd®). This agent is an ophthalmic preparation used for external ocular infections. With the exception of burns, there are few, if any, adverse reactions; it is available in solution and ointment forms.

(4) Mafenide (Sulfamylon®).

(a) This is a topical agent used to prevent colonization of both gram positive and gram negative organisms in second and third degree burns.

(b) It causes intense pain at the application site, and carbonic anhydrase is inhibited causing metabolic acidosis.

(5) Silver Sulfadiazine (Silvadene®).

(a) This agent is used in the same manner as that described in (4) above. In addition, it is very effective against yeast organisms.

(b) Adverse reactions to this agent are infrequent and are limited to localized burning, rash, and itching.

(6) Vaginal products. These products are used in the treatment of vaginal infections caused by a variety of organisms. They are available either as suppositories or as creams. The most frequent adverse reaction to these products is localized vaginal itching. These products are available as AVC® or Sultrin®.

(7) Urinary analgesics.

(a) This class of drugs is not related to sulfonamides, but is often used in conjunction with them in the treatment of urinary tract infections. They reduce the pain caused on urination and the itchy feeling associated with the infection.

(b) These compounds are azo dyes, and their use may discolor the urine or feces.

(c) The most commonly used urinary analgesic is phenazopyridine (Pyridium®).

Continue with Exercises

EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Antipseudomonal activity is first found in what generation of cephalosporins?

   a. First generation.

   b. Second generation.

   c. Third generation.

2. Beta lactamase resistant activity is found in what generation of cephalosporins?

   a. First generation.

   b. Second generation.

   c. Third generation.

For exercises 3 through 7, match the letter of the trade name in column I with its corresponding generic name in Column II.

Column I	Column II
3. Spectinomycin	a. Geopen®
4. Cefazolin	b. Wycillin®
5. Cefoxitin	c. Trobicin®
6. Carbenicillin disodium	d. Vibramycin®
7. Procaine penicillin G	e. Mefoxin®
	f. Geocillin®
	g. Ancef®

For exercises 8 through 10, match the drug name or category in Column I with its corresponding side effect in Column II.

Column I	Column II
8. Erythromycin	a. Nephrotoxicity, ototoxicity
9. Aminoglycosides	b. Localized vaginal itching
10. Sultrin®	c. Photosensitivity
	d. Cholestatic hepatitis
	e. Discoloration of teeth

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 3

1. c (para 3-9h)
2. b (para 3-9g)
3. c (para 3-12j)
4. g (para 3-9f(4))
5. e (para 3-9g)
6. a (para 3-8d(4))
7. b (para 3-8a(8))
8. d (para 3-10d)
9. a (para 3-12c)
10. b (para 3-17h(6))

End of Lesson 3

LESSON ASSIGNMENT

LESSON 4 Antifungals, Antihistamines, and Antimalarial Agents.

TEXT ASSIGNMENT Paragraphs 4-1 through 4-15.

LESSON OBJECTIVES After completing this lesson, you should be able to:

4-1. Given the trade or generic name of a drug used to treat fungi, select the fungus or fungi treated with that drug.

4-2. Given the trade or generic name of a drug used to treat fungi, select the side effects associated with the use of the given drug.

4-3. Given the trade name of a drug used to treat allergies, select the generic name that corresponds to the trade name.

4-4. Given a list of uses of drugs, select the uses for antihistamines.

4-5. Given the name of an antihistamine, select the use for that antihistamine.

4-6. Given the trade or generic name of an antihistamine, select the uses, cautions, warnings, or adverse reactions for the drug.

4-7. Given the trade or generic name of a drug used to treat malaria, select the form of malaria treated with that drug.

4-8. Given the name of an antimalarial agent, select the side effects, caution, or warning associated with that agent.

4-9. Given the name of an antifungal antihistamine or antimalarial agent, select the route of administration that can be used for that drug.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 4

ANTIFUNGALS, ANTIHISTAMINES, AND ANTIMALARIAL AGENTS

Section I. ANTIFUNGALS

4-1. INTRODUCTION

A fungus is a plant-like organism of the same class to which mushrooms and molds belong. They are everywhere in our environment, and those that cause systemic infection are often geographically limited. Although fungi are common plant pathogens, only about 50 of the thousands of known species are pathogenic to humans. An antifungal is an agent that destroys or prevents the growth of fungi. Some agents are used topically while others are used systemically. The successful treatment of fungal infections depends on accurate identification of the offending fungus, followed by proper selection and use of an antifungal drug. Most superficial infections can be adequately treated with topical therapy. Deep seated infections of the hair or nails generally require systemic therapy. Systemic fungal infections require the use of orally or intravenously administered drugs, some of which are toxic.

4-2. SPECIFIC AGENTS

Various drugs are used to treat fungus.

a. **Tolnaftate (Tinactin®).** This agent is a topical antifungal and is used in the treatment of athlete's foot, jock itch, and ringworm. The dosage of the drug depends on the extent of the affected area. Tolnaftate is available as a solution, cream, powder, and aerosol powder. All containers should be labeled "FOR EXTERNAL USE ONLY."

b. **Nystatin (Mycostatin®).** Nystatin is active in vitro against a number of yeasts and molds that cause "diaper rash," thrush, and vaginal candidiasis. Nystatin is relatively nontoxic, but nausea, vomiting, and diarrhea may occur with oral therapy. This drug has staining properties, and patients using the drug should be cautioned. Nystatin is available as an ointment, in oral suspension, vaginal cream, vaginal tablets, and oral tablets.

c. **Undecylenic Acid (Desenex®).** This drug is an antifungal agent employed in the treatment of superficial fungus infections of the skin. Since it is only fungistatic and not fungicidal, attention must be given to other forms of hygiene. This agent may cause irritation on raw lesions; therefore, astringents are used to assist in reducing the rawness and irritation. An example of such an astringent is zinc, which may be incorporated into ointments, powders, and aerosols.

d. **Griseofulvin (Gris-Peg®).** This agent is very effective in the treatment of superficial fungus infections. It is fungistatic, not fungicidal, and is administered systemically with the dosage varying with the severity and type of infection. Griseofulvin may cause nausea and vomiting, which may be avoided by taking the drug with or shortly after a meal. Headaches are also relatively frequent. This drug is available in tablets, capsules, and in suspension.

e. **Ketoconazole (Nizoral®).** This drug is a broad-spectrum synthetic antifungal agent. It is used as a systemic agent in the treatment of candidiasis, oral thrush, histoplasmosis, and blastomycosis. Ketoconazole may produce nausea and vomiting. Occasionally, potentially fatal liver disorders may occur unless they are properly recognized and managed. The agent should be taken with meals; the patient should be cautioned against using antacids and other drugs that inhibit gastric acid, as gastric acid is necessary for the absorption of ketoconazole. This drug is available only in tablet form.

f. **Selenium Sulfide (Selsun®).** This agent is a topical antifungal used in the treatment of dandruff and seborrheic dermatitis. Oiliness or dryness of the scalp and hair may occur following use, and there have been reported cases of increased normal hair loss. This agent may also discolor the hair; thorough rinsing of the hair can minimize discoloring. Selsun, a prescription drug, is intended for external use only, as is Selsun Blue, an over the counter product.

g. **Clotrimazole (Lotrimin®).** This drug is a broad spectrum antifungal effective as a topical agent in the treatment of infections caused by pathogenic fungi and in the treatment of infections caused by Candida albicans. Side effects associated with the use of this product include itching, burning, peeling, blisters, and erythema. When used as a vaginal cream, it may cause staining of undergarments. Clotrimazole is available in tablets, creams, and in solution.

h. **Miconazole Nitrate (Monistat-Derm®, Monistat-7®).** Miconazole is a synthetic antifungal effective against the common skin fungi and vaginal candidiasis. The side effects for miconazole are the same as for clotrimazole. This product is available in cream form for either topical or vaginal application, vaginal suppositories, lotions for topical application, and in an injectable form.

i. **Fluconazole (Diflucan®).** Fluconazole is a synthetic broad-spectrum antifungal agent. It is used in the treatment of candidiasis and cryptococcal meningitis. The side effects include nausea, vomiting, headache, skin rash, abdominal pain, and diarrhea. Additionally, fluconazole has several significant drug interactions. Diflucan is available as tablets, powder for suspension, and injection.

j. **Econazole (Spectazole).** Econazole is a topical antifungal that is used to treat tinea cruris, T. pedis, T. corporis, T. rubrum and T. versicolor. Side effects include burning, itching, and stinging. Spectazole is available as a one-percent cream that is applied once to twice daily.

k. **Amphotericin B (Fungizone®).** This agent is an antibiotic with antifungal activity and is used both topically and systemically. Amphotericin B may exert a "drying" effect on the skin, and in some cases, may stain the nails. This drug is available as a cream, ointment, and parenteral injection.

Section II. ANTIHISTAMINES

4-3. INTRODUCTION

Surely, you know several people who are allergic to pollen, feathers, dogs, and other things. These people may break out in hives, sneeze, or have runny noses and other conditions consequently. These symptoms are annoying, but some allergic reactions can prove to be fatal, as in the case of anaphylactic shock, which can lead to death in a few minutes. The group of drugs known as antihistamines is used primarily in allergic reactions, as sedatives, and in the treatment of certain specified disorders. To fully understand the action of these drugs, it is necessary to look at allergies and how they are caused.

4-4. IMPORTANT TERMS AND DEFINITIONS PERTAINING TO ALLERGIES

a. **Allergy.** Allergy is defined as the abnormal or altered reaction to an antigen. Certain individuals have an excessive or exaggerated sensitivity to a substance that does not affect a normal individual. Allergy may also be thought of as a side effect of immunity. In immunity, the antigen-antibody reactions take place in the circulatory system. In allergy, however, the antigen antibody reactions take place in contact with the cells.

b. **Allergic Reaction.** The allergic reaction begins with the introduction of an antigen into the body of an individual. Abnormal (incomplete univalent) antibodies are then formed by the plasma cells and are found in great numbers around tissue cells. When the antigen is again introduced into the body, the antigen antibody reaction occurs in contact with the cells. This reaction damages cells, the cells swell and burst; consequently, large amounts of a chemical called histamine, are released in the body. Mast cells, which contain large amounts of histamine, are found around capillary walls. These cells are particularly susceptible to damage caused by the antigen antibody reaction.

4-5. IMPORTANT CONSIDERATIONS ABOUT ALLERGIC REACTIONS

a. **Effects of an Allergic Reaction.** An allergic reaction has several effects on the body. These effects occur mainly because of the large concentration of histamine that is released. Peripheral vasodilatation occurs, and capillaries become more permeable. Here, blood plasma "leaks" from the capillaries; the capillary blood volume drops because peripheral vasodilatation and increased permeability of the capillaries. Consequently, there is a decrease in blood pressure. Bronchoconstriction, which can interfere greatly with breathing, may occur. The histamine release may also cause severe rash or hives.

b. **Types of Allergic Reactions.** There are several types of allergic reactions. One type of allergy is the mild local reaction to general antigens. These reactions are not severe. The antigen producing the reaction can be anything from chicken egg white to horse dander. Allergic rhinitis is an antigen antibody reaction with symptoms occurring in the nasal mucosa. When the antigen is pollen, then it is called hay fever. Hay fever is characterized by edema (swelling), sneezing, itching, and increased mucous secretions. Asthma is characterized by bronchoconstriction as well as wheezing, dyspnea, and coughing. The cause of asthma is frequently an allergic reaction to airborne antigens (it may also be caused by non-allergy related factors). Urticaria (or hives) is characterized by wheals (edema), erythema, and itching of the skin. Foods, drugs, clothing, parasites, and many other substances may cause urticaria.

c. **Allergic Reactions from Drugs.** Allergy can also involve mild local and systemic drug hypersensitivity reactions. The drugs that commonly cause these reactions include biologicals and antibiotics. Hives (urticaria) (swollen red areas on the skin) and swollen eyelids and lips are outstanding features here. In addition, swelling and pain that occur in joints and muscles when a patient is taking a drug, it is a possible indication the patient is allergic to the drug. An elevated temperature is the third indication that an allergic reaction may be occurring. The lymphatic hypersensitivity reaction is swelling. The respiratory system reaction is bronchoconstriction, while the nasal reaction is a runny nose. Jaundice is a symptom of the hepatic reaction, while vasodilation and increased permeability of the blood vessels are the circulatory system hypersensitivity reaction.

d. **Systemic Reactions from Drugs.** In addition, systemic reactions occur whenever a drug or an antigen that reacts with abnormal anti-bodies is introduced into the body. One type of systemic reaction is serum sickness. The signs and symptoms of mild drug hypersensitivity and serum sickness may be identical. Serum sickness occurs several days after an injection of a foreign protein, such as horse serum, into a patient that is not already immune. Antibodies are not released into the tissues until 7 to 10 days later. After this period, the reaction between the newly formed antibodies and the still present protein of the horse serum results in an allergic reaction throughout the body. It is similar to anaphylaxis, except in serum sickness the reactions are slow in occurring. The patient usually recovers without complications.

e. **Anaphylactic Shock.** Anaphylactic shock is the most serious type of allergic reaction. The antigen that produces the response can range from a bee sting toxin to an antibiotic. Again, this response is produced by an antigen-antibody reaction characterized by the sudden overwhelming release of histamine in the body. Therefore, one would expect the effects of histamine on the body to be demonstrated. Two main effects of anaphylactic shock on the body are severe drops in blood pressure and impaired respiration. The drastic drop in blood pressure develops from the severe peripheral vasodilation and the increased permeability of the capillaries. The impaired breathing arises from bronchoconstriction. The anaphylactic reaction occurs very rapidly after the introduction of the antigen into the patient. Unless prompt action is taken by medically trained personnel, the patient will die in a matter of minutes.

f. **Prevention or Control of Symptoms of Allergic Reactions.** It is possible to decrease or even prevent the symptoms of an allergic reaction. For a very severe allergic reaction like anaphylactic shock, a drug that will stop the effects of histamine on the body must be used. Moreover, the drug must produce positive physiological effects on the body. The drug used for anaphylactic shock is epinephrine.

g. **Desensitization.** In some instances, it may be advantageous to prevent an allergic reaction from occurring. Since the production of abnormal antibodies by the plasma cells is the real beginning of the potential allergic reaction, it makes sense that if the abnormal antibodies were not produced, a reaction would not occur when the antigen again enters the body. The answer would then be to have only complete (divalent) antibodies produced in the body. This is the basis of treatment to prevent an allergic reaction. The treatment is referred to as desensitization. Here, extracts of substances such as pollen or drugs are given to the patient in small, but increasing doses. In time, the body produces complete antibodies, and the allergic reaction does not occur.

4-6. MECHANISM OF ACTION OF ANTIHISTAMINES

a. Antihistamines are drugs that compete with histamines for their receptor sites, known as H1 and H2 receptor sites. These receptor sites are found in tissue cells, with H1 receptors located throughout the body and H2 receptor sites found in the gastric mucosa. The majority of available antihistamines are H1 antagonists.

b. H1 antagonists are believed to act not by opposing but by preventing the physiologic action of histamine. This occurs because anti-histamine molecules are chemically similar to histamine molecules. When the antihistamine binds itself to the H1 receptor site, it prevents histamine from doing the same, which effectively eliminates histamine action.

4-7. INDICATIONS FOR USE OF ANTIHISTAMINES

The antihistamines are used primarily in allergic reactions, as sedatives, and in the treatment/prevention of motion sickness and drug-induced Parkinsonism. These preparations do not immunize the patient or protect him over a long period. Their benefits are comparatively short-lived, provide only symptomatic relief, and do not correct the underlying disorder.

4-8. CAUTIONS AND WARNINGS

The most common side effect of these preparations is drowsiness, which may become so marked that deep sleep occurs. Other reactions include dizziness, dryness of mouth and throat, nausea, muscular weakness, and gastrointestinal disturbances. Patients receiving these products should be cautioned against drinking alcohol to avoid the associated drowsiness.

4-9. GENERAL ANTIHISTAMINE PREPARATION

a. **Diphenhydramine (Benadryl®).** This preparation is used for its antihistamine, anti-Parkinson, and sedative properties. The usual dose varies according to the age of the patient and the condition being treated. Diphenhydramine is available in capsules, as an elixir, or in an injectable form.

b. **Chlorpheniramine (Chlor-Trimeton®).** This product is used exclusively for its antihistamine properties. It is available in tablets and as syrup.

c. **Loratadine (Claritin) and Fexofenadine (Allegra).** These products are used to treat allergic reactions such as seasonal allergies. They do not cause drowsiness

d. **Additional Products.** Other antihistamines commonly available include Brompheniramine (Dimetane®) and promethazine hydrochloride (Phenergan®). These products have similar properties, side effects, and dosage forms.

4-10. COMBINATION PREPARATION

a. **Brompheniramine, Phenylpropanolamine (Dimetapp®).** This product is used for its antihistaminic and decongestant properties. The dose depends on the form in which it is taken and the patient's age. It is available in tablet and elixir form.

b. **Other Preparations.** Other combination preparations that are available include dexbrompheniramine and pseudoephedrine (Drixoral®), triprolidine and pseudoephedrine (Actifed®), and phenylpropanolamine and chlorpheniramine (Ornade®).

4-11. ANTIPRURITIC PREPARATIONS

a. **Cyproheptadine (Periactin®).** This drug is used to control itching caused by allergic reactions. It causes drowsiness and should not be taken with alcohol. Periactin® is available in tablet and syrup form.

b. **Other Preparations.** Other antipruritic preparations include trimeprazine tartrate (Temaril®) and hydroxyzine hydrochloride (Atarax®).

4-12. HISTAMINE INHIBITORS

a. Cromolyn sodium (Intal®) is a successful anti-asthma prophylactic drug that was produced as a result of knowledge of the mechanisms of allergic reactions. It acts by inhibiting the granulation of pulmonary mast cells, thereby preventing the release of histamine responsible for causing asthmatic symptoms; it has no value in stopping an allergic attack already in progress.

b. Cromolyn sodium is administered by inhalation and is used in the management of patients with severe bronchial asthma. It is also indicated in certain patients to prevent exercise-induced bronchospasm.

c. Following therapy, cromolyn sodium may cause mild throat irritation, coughing, and hoarseness. On occasion, it has been known to produce bronchospasms. Esophageal irritation is relieved by antacids or by drinking a glass of milk before each treatment to protect the gastrointestinal mucosa from direct contact with the drug. The drug demonstrates a low level of toxicity, but some hypersensitivity and allergy have occurred.

4-13. H2 ANTAGONISTS

a. Cimetidine (Tagamet®) is an antihistamine that selectively and competitively inhibits the action of histamine by occupying the H2 receptors of the gastrointestinal mucosa. This action inhibits basal gastric ulcers and controls pathogenic hypersecretory conditions.

b. The drug is available in tablet and syrup form for oral administration or may be administered intramuscularly or intravenously. It may be essential to administer antacids with cimetidine as needed for relief of pain. However, they should not be given simultaneously.

c. Side effects include mild transient diarrhea, muscular pain, dizziness, and skin rashes. A few cases of reversible confusion states have been reported in the elderly, probably because of overdose. Mild gynecomastia been observed in patients treated with this drug for one month or longer. It is relatively nontoxic. Cimetidine does not cause drowsiness like the H1 antagonists.

Section III. ANTIMALARIAL AGENTS

4-14. INTRODUCTION

Malaria has been a critical problem for the American fighting man for decades. Even with the pharmacological advances of today's modern medicine, strains of resistant malaria are now rapidly spreading throughout endemic areas of the world. The treatment of malaria requires extensive chemotherapy that is aimed at interrupting the life cycle of the disease in man.

4-15. SPECIAL AGENTS

Several significant drugs have successfully treated forms of malaria. The agents listed below work on either the blood or liver stages of malaria.

a. **Chloroquine (Aralen®).** This drug acts only on the blood stages of the parasite. It is the drug of choice for treatment of acute attacks in all types of malaria except drug resistant strains of P. falciparum. Chloroquine is also very effective in the prophylaxis of malaria. Side effects associated with the use of this agent are gastrointestinal disturbances, anal pruritis, and visual disturbances. The visual disturbances occur with prolonged use of the drug, which causes damage to the cornea and retina.

b. **Primaquine.** Primaquine is an antimalarial agent used for the radical cure of the relapsing forms of malaria caused by P. vivax or P. ovale. It is effective against these types of malaria because it acts on the tissue stages of the parasite in the liver. It is the presence of the parasite in the liver which, when not treated, may cause relapses of the disease. The main side effect associated with this drug is hemolytic anemia. This condition is frequently seen in patients lacking the G-6-PD enzyme, a genetic defect that often occurs in dark skinned individuals and those of Mediterranean descent. GI upset and visual disturbances have also occurred.

c. **Chloroquine and Primaquine® (CP®).** This agent is a combination drug suitable for prophylaxis (prevention) of all types of malaria. Chloroquine and Primaquine® should not be given for acute attacks due to severe primaquine toxicity if more than 26.3 mg of primaquine is given daily. Chloroquine and Primaquine® tablets are no longer the drug of choice for routine prophylaxis of malaria. The side effects of CP® are the same as those for the individual ingredients.

d. **Pyrimethamine and Sulfadoxine (Fansidar®).** This combination is used in the prophylaxis and treatment of malaria caused by organisms resistant to chloroquine. Some of the side effects associated with this drug are hemolytic anemia and gastrointestinal irritation. This drug should not be dispensed to pregnant or lactating women.

e. **Quinine.** Quinine is an alternative drug in the treatment of malaria strains resistant to other modes of treatment. This agent acts only on the blood stages of the parasite. Side effects include gastrointestinal irritation, tinnitus, vertigo, headache, and drug hypersensitivity.

f. **Doxycycline (Vibramycin®).** Doxycycline is use prophylactically for P. falciparum in short-term travelers to areas with chloroquine resistant strains. Side effects include GI upset and superinfection.

Continue with Exercises

EXERCISES, LESSON 4

INSTRUCTIONS: Answer the following items by marking the lettered response that best answers the item or completes the statement.

After you have completed all of these items, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions.

1. Tolnaftate (Tinactin®) is used for the treatment of:

   a. Athlete's foot.

   b. Jock itch.

   c. Ringworm.

   d. All of the above.

2. Selenium sulfide is used for the treatment of:

   a. Diaper rash.

   b. Dandruff.

   c. Vaginal candidiasis.

   d. All of the above.

3. Cimetidine is used for the treatment of:

   a. Mild allergic reactions.

   b. Severe allergic reactions.

   c. Gastric ulcers.

   d. Thrush.

4. Chloroquine and primaquine tablets (CP® tablets) are used in the treatment of active attacks of what type of malaria?

   a. P. falciparum.

   b. P. vivax.

   c. All types of malaria.

   d. Not used to treat active malaria.

5. A patient receiving antihistamines should be cautioned about:

   a. Taking the medication with food or milk.

   b. Avoiding antacids.

   c. Avoiding iron preparations.

   d. Drowsiness.

6. A patient taking cromolyn sodium (Intal®) might have the following side effects.

   a. Throat irritation.

   b. Coughing.

   c. Hoarseness.

   d. All of the above.

7. Which of the following is a side effect of Fansidar®?

   a. Hemolytic anemia.

   b. Drowsiness.

   c. Cough.

   d. All of the above.

8. Antihistamines are used for:

    a. Treatment of allergic reactions.

    b. Sedatives.

    c. Treatment/prevention of motion sickness.

    d. All of the above.

9. Cromolyn sodium is used to treat:

    a. Anaphylactic shock.

    b. Asthma.

    c. Motion sickness.

    d. Drug induced Parkinsonism.

10. Which of the following is used for its antipruritic activity?

    a. Cyproheptadine.

    b. Trimeprazine tartrate.

    c. Hydroxyzine hydrochloride.

    d. All of the above.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 4

1. d (para 4-2a)
2. b (para 4-2f)
3. c (para 4-13a)
4. d (para 4-15c)
5. d (para 4-8)
6. d (para 4-12c)
7. a (para 4-15d)
8. d (para 4-7)
9. b (para 4-12b)
10. d (para 4-11)

End of Lesson 4

LESSON ASSIGNMENT

LESSON 5	Biologicals.
TEXT ASSIGNMENT	Paragraphs 5-1 through 5-13.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

5-1. Given the definition of a type of immunity, select the type of immunity to which it applies.

5-2. Given the name of a disease or condition and a list of biological agents, select the agent used to treat or prevent that disease or condition.

5-3. Given the name of a biological agent and a list of types of biological preparations, select the type of preparation represented by the biological agent.

5-4. Given the name of a biological agent and a list of storage requirements, select the storage requirements for that agent.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 5

BIOLOGICALS

5-1. INTRODUCTION

Many years ago, individuals became hysterical whenever anyone in the neighborhood contracted diseases like poliomyelitis or smallpox. Children were not allowed to leave their homes for fear of contracting these diseases. Today, however, we do not fear these diseases because of our knowledge of the benefits of immunization. Although you may not have appreciated it as a child, those "shots" you received from the doctor enabled you to resist many childhood diseases. As a Service Member, immunizations you received on a regular basis or received before entering a specific overseas area kept you free from disease and enabled you to accomplish the mission.

5-2. NATURAL RESISTANCE

a. **Species Resistance.** Species resistance is the ability of a particular species to resist the disease of another species and is physiological in nature. It has been observed that warm-blooded animals rarely exhibit microbial diseases associated with cold-blooded animals. One example of this species resistance is demonstrated by distemper, an often fatal disease in dogs, which rarely, if ever, affects man.

b. **Racial Resistance.** Racial resistance means that some races of people are less susceptible to some diseases than other races. Racial resistance is affected by heredity, customs, hygiene, and survival rates. An example is that blacks in West Africa are likely to have a deficiency of the enzyme G6PD. These individuals also have a resistance to falciparum malaria.

c. **Individual Resistance.** Many of us have individual resistance, another type of natural resistance to disease. Some individuals resist colds, flu, and other diseases to a greater degree than others. Some factors that contribute to this phenomenon are personal hygiene, state of nutrition, and of course, exposure to pathogenic organisms.

5-3. ACQUIRED RESISTANCE

a. **Acquired Resistance.** Acquired resistance is the ability of the body to overcome specific diseases or disorders after prior contact with the causative agent. An antigen is a foreign substance to the body that may be composed of lipid, protein, or carbohydrate material. Antibodies are specific substances formed by the body in response to stimulation by antigens. Antibodies are formed by plasma cells.

b. **Primary Response.** The first time an antigen enters the body, it initiates the production of a small number of antibodies. This is called the primary response.

c. **Secondary Response.** The next time the same antigen enters the same body, it stimulates a rapid increase in the production of a large number of antibodies. This is called the secondary response.

d. **End Result.** When the antigen is reintroduced into the body, antibodies react with the antigens by several mechanisms that either inactivate or destroy the antigen. The end result is that the antigen is unable to harm the body.

e. **Antigen-Antibody Reactions.** There are four types of antigen-antibody reactions that occur in the body.

(1) Agglutination occurs when antibodies attach one bacterium to another. The bacteria then form one large mass. This massing effect not only prevents tissue invasion by the bacteria, but also makes them more susceptible to phagocytosis.

(2) The second reaction, precipitation, occurs when antigens, which are soluble in plasma, are attached to one another by antibodies. When enough antigens and antibodies are combined, they form a solid mass that is insoluble and thus precipitates out of solution. The insoluble particles are then engulfed and digested by phagocytes.

(3) The third reaction is neutralization. Antibodies attach themselves to the reactive sites of antigens that have entered the body. Consequently, the toxin is neutralized and can no longer harm the body. The antigen-antibody complex is then engulfed by phagocytes. This process works well on both toxins and viruses.

(4) The fourth reaction is referred to as lysis of the organism. Here, antibodies attach themselves to bacteria, viruses, or other foreign cells. When the antibodies react with these cells, complement, a substance present in blood plasma, penetrates the cell membrane of the organism, which causes it to rupture.

5-4. ACTIVE IMMUNITY

a. **Active Imunity.** Active immunity results when antibodies are produced by the body as a result of stimulation by living, dead, or attenuated organisms or their toxins. Immunity of this type develops slowly and become effective in several weeks. Usually, active immunity is both complete and enduring.

b. **Types.** Active immunity can be divided into two types. First, natural active immunity is antibody formation stimulated by the presence of living organisms or their products that cause disease. In other words, you get the disease. Life-long immunity usually results from having a disease in which natural immunity can result. Second, artificial active immunity is antibody formation stimulated by the administration of a vaccine.

5-5. PASSIVE IMMUNITY

a. **Passive Immunity.** Passive immunity differs from active immunity in that antibodies from one person are given to another. In other words, antibodies produced by active immunization in one person are transferred to a susceptible person. This type of immunity provides immediate protection of short duration.

b. **Natural Passive Immunity.** Natural passive immunity is the process by which antibodies are transferred to a baby from an immune mother by placental transfer. This process forms complete, but temporary, immunity which may last from 6 to 12 months.

c. **Artificial Passive Immunity.** Artificial passive immunity is conferred by injecting blood serum from an immune human into a susceptible person. This is used to provide immediate protection in cases of known exposure or in the case of epidemics. Complete protection is assured for 2 to 3 weeks.

5-6. VACCINES

a. **Biologicals.** The biologicals, or vaccines, are used as an artificial means to augment the human resistance system to infectious organisms. Vaccines are dead or living (but attenuated) suspensions of bacteria, rickettsiae, or viruses. In the preparation of vaccines of living organisms, care must be taken to ensure that the vaccine will cause antibody production, but not the disease itself. This is accomplished by reducing the virulence of the microorganism through a multi-step dilution procedure.

b. **Bacterial Vaccines.** For the most part, bacterial vaccines are killed suspensions of millions of the organism. For example, cholera vaccine is a suspension containing eight billion killed Vibrio cholerae organisms per milliliter.

c. **Protective Antibody Formation.** The first attempt to induce protective antibody formation in an individual was carried out by an English physician, Edward Jenner, in 1796. Jenner inoculated an 8-year-old boy with pustular material from a cowpox infection on the hand of a dairymaid. The boy experienced mild symptoms of cowpox for about 8 days, then recovered completely. Later attempts to infect him with the smallpox failed. This event is considered a major medical contribution; the last naturally acquired case of smallpox in the world occurred in 1977. Global eradication was certified two years later and confirmed in 1980 by the World Health Assembly.

5-7. GENERAL PRECAUTIONS

a. **Screen.** Before a patient receives an immunization, certain precautions need to be taken. The patient should be screened for possible allergies to the vaccine to be used. Skin tests for sensitivity to horse serum antitoxins and antiserums should be done prior to administration.

b. **Waiting Period.** An anaphylactic tray containing the necessary drugs should be available in the immunization area. Patients should be instructed to wait in the immediate area for 30 minutes following an injection to guard against a possible allergic reaction.

c. **Check Expiration Date.** The expiration date of all biological products should be checked before each use. Biologicals requiring reconstitution should be used immediately after introduction of the diluent. All suspensions should be well shaken to ensure even distribution of organisms within the suspension. All biologicals should be stored properly when not in use.

d. **Prevention of Secondary Infections.** All injections should be administered following standard aseptic techniques to prevent secondary infections.

e. **Precautions.** Individuals with a defective or altered immune mechanism should not be given a live virus vaccine. Additionally, individuals with acute febrile illness and pregnant women should NEVER receive a live virus vaccine.

5-8. BACTERIAL VACCINES

a. **Inactivated (Killed) Vaccines.**

(1) These suspensions consist of suspensions of killed whole bacteria. These vaccines are most often used to protect those who travel outside the United States.

(2) Examples of these agents include plague, cholera, typhoid, and anthrax vaccines.

b. **Bacterial Live Vaccines.**

(1) These consist of suspensions of live attenuated bacteria that are proven to produce infection, but only in a mild self-limiting form. Thus, a mild planned infection is substituted for an unpredictable, possibly severe one. The most effective vaccines for the induction of active immunity are in this category.

(2) Examples of bacterial live vaccines include plague (also available as an inactivated bacterial virus) and tuberculosis.

(3)The protection provided by all bacterial vaccines, live or inactivated, is active immunity.

5-9. VIRAL VACCINES

a. These vaccines are comprised of killed or live attenuated organisms which are derived from culture medium containing living cells such as embryonated eggs, rabbit brain tissue, or monkey kidney tissue. These agents are used to develop active immunity.

b. Smallpox vaccine consists of live attenuated virus derived from calf lymph. In the Army, it is available as a freeze-dried powder for reconstitution. A successful vaccination produces a limited cutaneous infection with minimal systemic involvement.

c. Oral polio (Sabin) vaccine contains live attenuated poliovirus grown in monkey-kidney-tissue culture or human cell culture. This vaccine is the agent of choice against polio because of its ease of administration, and it produces immunity resembling that induced by natural poliovirus infection. It is available in both monovalent and trivalent form. This vaccine should be stored in a freezer (-9 to -14°C).

d. Rabies vaccine is prepared from fixed rabies virus in human diploid embryonic cell cultures. It is the agent of choice for post-exposure prophylaxis for rabies and indicated for pre-exposure prophylaxis for high-risk individuals. Prophylaxis against rabies in persons exposed to rabies through animal contacts includes both passive immunization with rabies immune globulin to provide immediate protection and active immunization to stimulate endogenous rabies antibody formation. The dried vaccine should be stored in a refrigerator (2-8°C) and reconstituted with the accompanying diluent prior to use.

e. Live attenuated virus grown in embryonated chicken eggs and dispensed in lyophilized form makes up Yellow Fever vaccine. It produces an asymptomatic infection and solid immunity to natural infection and disease for 10 years or more.

f. Rubella vaccine is available as a lyophilized powder that must be stored under normal refrigeration (2 to 8°C) and reconstituted with a special diluent. It is used in children between 1 year of age and puberty and in women of childbearing age who have not demonstrated adequate antibody protection. These women must agree to take measures to prevent pregnancy for 3 months following the administration of the vaccine; birth defects can occur as a result of receiving the Rubella vaccine during the first few months of pregnancy.

g. Mumps vaccine is a live viral vaccine which provides protection which may last up to 10 years. Immunization against mumps is indicated in children 15 months of age or older and adults (based on individual evaluation of patient needs). The vaccine should be stored in a refrigerator (2 to 8°C) and reconstituted with the accompanying diluent prior to use; it must be used within 8 hours of reconstitution.

h. Measles vaccine is a live attenuated virus vaccine. It produces a modified infection in susceptible individuals; it should not be used by individuals with egg allergies. Rubeola vaccine should be stored under normal refrigeration; the lyophilized powder must be reconstituted before use and used within 8 hours.

i. Various strains of influenza vaccine, usually mixed, are freshly prepared each year. It appears that the immunity offered by these vaccines does not exceed 4 months. The vaccines are prepared in ten-day incubated, embryonated chicken eggs, give artificial active immunity, and must be stored under normal refrigeration.

j. Viral vaccines in combination are available for simultaneous immunization against more than one disease. Two common agents are the mumps and rubella vaccine and the measles, mumps, and rubella (MMR) vaccine. Information concerning the individual vaccines applies to combination products.

5-10. TOXOIDS

a. Among the most deadly of man's enemies are the toxins. Seven ounces of pure crystalline botulinus toxin would kill every human now on the face of the earth. A major source of this toxin is improperly prepared home canned vegetables, especially green beans.

b. The toxoids are prepared from the exotoxins of bacteria by treating with formaldehyde and then purifying them. This results in a material that has lost its toxic properties but maintains the antigenic specificity of the active toxin. Toxoids produce artificial active immunity.

c. Tetanus toxoid is used to immunize individuals against the possibility of tetanus, is highly effective, and produces an immunity that lasts for 10 years or more. Additional boosters are administered following injuries where the tetanus bacterium may be present.

d. Diphtheria and tetanus toxoid (pediatric type) is used for primary immunization and booster injections in children up to 6 years of age. This agent is used when pertussis vaccine must be given separately or is omitted. Diphtheria and tetanus toxoid, adsorbed (adult type), is used for primary immunization and booster injections in adults and children over 6 years of age. The adult type is 1/10 the strength of the pediatric type.

e. Diphtheria, tetanus, and pertussis vaccine (DPT) is a combination product recommended for the primary immunization and booster injections of all children under 6 years of age. This biological is NOT recommended for children over 6 years of age or adults.

5-11. IMMUNE SERUM GLOBULINS

a. These agents are employed to lessen the symptoms of infectious disease or to provide prophylaxis against communicable disease in endemic areas. They are prepared from the blood of humans that have recovered from known attacks of the disease or have been immunized against the disease with large doses of toxoids. These agents produce passive immunity.

b. Tetanus immune globulin is a sterile solution of globulins obtained from the plasma of adults hyperimmunized with tetanus toxoid. It is an effective prophylactic agent in patients with wounds potentially contaminated with Clostridium tetani.

c. Immune serum globulin consists primarily of IgG antibodies and represents the gamma globulin fraction of normal human plasma. It is used to prevent infections such as hepatitis or measles in exposed, susceptible individuals. This product should be stored under normal refrigeration.

d. Rabies immune globulin consists of antibodies from the serum of individuals repeatedly vaccinated against rabies.

5-12. ANTITOXINS

These agents are prepared by injecting animal sources with purified toxin or toxoid and extracting and processing the blood. Antitoxins are used with caution because of their high incidence of hypersensitivity reactions from equine sources. Some examples of these agents are tetanus antitoxin (equine), botulism antitoxin (equine), and diphtheria antitoxin (equine). Antitoxins also produce passive immunity.

5-13. ANTIVENIN (CROTALIDAE) POLYVALENT

a. This agent is a sterile preparation derived by drying a frozen solution of specific venom-neutralizing substances obtained from the serum of healthy horses immunized against venom of four species of pit vipers.

b. The smaller the patient, the larger the initial dose that is required. The amount of antivenom that can be administered is virtually unlimited. This provides passive immunity.

Continue with Exercises

EXERCISES, LESSON 5

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or complete the statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions.

For exercises 1 through 5, match the type of biological preparation in Column I with its corresponding agent in Column II.

Column I	Column II
1. Oral polio	a. Viral vaccine
2. Plague	b. Bacterial vaccine
3. Measles	c. Toxoid
4. Rabies Immune Globulin	d. Immune serum globulin
5. Rubella	e. Antitoxin

For exercises 6 through 10, match the type of immunity in Column I with its corresponding type of biological in Column II,

Column I	Column II
6. Vaccine	a. Active immunity
7. Toxoid	b. Passive immunity
8. Immune serum globulin	
9. Antitoxin	
10. Antivenin	

11. Antivenin (Crotalidae) Polyvalent is used to treat the following condition:

    a. Rabies.

    b. Pit viper bite.

    c. Rubella.

    d. Tetanus (from puncture wound).

    e. Malaria.

12. Oral polio (Sabin) vaccine has to be stored under which of the following conditions?

    a. In a refrigerator (2 to 8).

    b. At room temperature.

    c. In a freezer (-9 to-14).

    d. In a lyophilized (freeze-dried) powder.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 5

1. a (para 5-9c)
2. b (para 5-8a(2))
3. a (para 5-9h)
4. d (para 5-11d)
5. a (para 5-9f)
6. a (para 5-8c)
7. a (para 5-10b)
8. b (para 5-11a)
9. b (para 5-12)
10. b (para 5-13b)
11. b (para 5-13a)
12. c (para 5-9c)

End of Lesson 5

LESSON ASSIGNMENT

LESSON 6	Vitamins and Minerals.
TEXT ASSIGNMENT	Paragraphs 6-1 through 6-4.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

6-1. Given the name of a vitamin or mineral and a list of body functions select the body function of that vitamin or mineral.

6-2. Given the name of a vitamin or mineral and a list of diseases and/or conditions, select the disease and/or condition associated with a deficiency of that vitamin or mineral.

6-3. Given the term water-soluble or lipid soluble select the vitamins that fall into each of these categories.

6-4. Given the name of a vitamin or mineral and a list of toxicities/adverse reactions select the toxicities/adverse reactions associated with that vitamin or mineral.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 6

VITAMINS AND MINERALS

6-1. INTRODUCTION

a. **Biochemical Importance.** Vitamins have great biochemical importance because they are essential for maintenance of normal metabolic function, growth, and health. The name vitamin means “vital for life.” Only a few vitamins are synthesized in the body. Thus, most vitamins must be ingested in food or in their pure form as dietary supplements. Only small amounts of vitamins are necessary for growth and health, and an adequate and varied diet will provide all the vitamins needed, except during pregnancy and infancy. Restricted diets as a result of cultural or idiosyncratic beliefs, alcoholism, poverty, ignorance, or disorders of the GI tract that interfere with absorption will lead to vitamin deficiency. In these cases, vitamin preparations are therapeutic.

b. **Oral Sources.** Oral sources of minerals may be found commercially, individually, or combined within a multivitamin and mineral combination. These minerals are inorganic constituents of foods and biological fluids and play a specific role as nutrients. The absence from the diet of only a few of these minerals has been shown to produce specific deficiency problems. A few are known to be involved in metabolic functions and are therefore possible dietary essentials.

c. **Vitamins.** Vitamins fall into two categories, lipid (fat) soluble or water-soluble. The lipid soluble vitamins are A, D, E, and K. Vitamins C and B complex are examples of water-soluble vitamins.

d. **Problems Associated with Excessive Vitamin Intake.** Most problems associated with excessive vitamin intake are related to fat-soluble vitamins because of retention in the body. Problems with excessive water-soluble vitamin intake are minimal because they are rapidly excreted in the urine.

6-2. LIPID-SOLUBLE VITAMINS

a. **Fat-Soluble Vitamins.** Fat-soluble vitamins are well absorbed from the normal GI tract. Bile is essential for absorption; therefore, biliary obstruction or hepatic disease may cause impairment of absorption.

b. **Fatty Deposits of Fat-Soluble Vitamins.** In general, fat-soluble vitamins will be stored in fatty deposits throughout the body. They may be excreted in the urine as water-soluble metabolites or in the feces, by biliary excretion.

c. **Vitamin A.**

(1) Vitamin A is essential for growth, especially in bone, reproduction, and embryonic development. It appears to be essential for the integrity of epithelial cells. It functions in the rods of the retina to form rhodospin that is necessary for night vision.

(2) Natural sources of vitamin A are milk, butter, eggs, green vegetables, liver, and kidney.

(3) Common deficiency states are night blindness, keratinization (scales), and dryness of the epithelium, particularly in the extremities, cornea, and conjunctiva. Toxicities seen in overdoses are relatively nonspecifics including irritability, vomiting, dry skin, pruritis, and loss of appetite, headache, gingivitis, and mouth fissure. Diagnosis of overdose is usually made following the appearance of tender, deep tissue swelling on the extremities and in occipital region of the head. Acute intoxication in infants is seen by an increase in intracranial pressure.

d. **Vitamin D.**

(1) Vitamin D facilitates the absorption of calcium from the small intestine, which is essential in the mineralization of bone and maintaining normal plasma calcium levels.

(2) A few natural sources of vitamin D are liver dairy products and fish. In adults, vitamin D deficiency is most likely to occur in times of increased calcium requirements (pregnancy and lactation). This results in “adult rickets” or osteomalacia, which is a decrease in bone density. Gross bone deformities occur only in advanced stages of the disease.

(3) In children, because of reduction in absorption of calcium and phosphate, the bones do not mineralize properly. Therefore, the bones are not able to support the body weight-giving rise to the deformities of rickets.

(4) Toxicity or overdose is usually the result of “mega vitamin” therapy. Initial signs and symptoms are those associated with hypercalcemia (weakness, fatigue, headache, nausea, vomiting, and diarrhea). Prolonged hypercalcemia may result in deposition of calcium salts in the soft tissues, most significantly in the kidney.

e. **Vitamin E.**

(1) There is much controversy over vitamin E therapy, but it appears to be essential for normal growth maintenance. A biological antioxidant protects unsaturated fatty acids and membrane structures. Natural diet sources include vegetable oils and wheat germ.

(2) Signs of edema and anemia have been seen in infants fed with commercial formulas low in vitamin E.

(3) Overdose toxicity appears as gastrointestinal distress. Two reports have shown possible thrombophlebitis, which was resolved after discontinuation of high dose vitamin E.

f. **Vitamin K (Phytonadione, Menadione, Menadiol).**

(1) Vitamin K promotes the hepatic biosynthesis of prothrombin, a component necessary for blood clotting. Sources of vitamin K are green leafy vegetables and vitamin K producing bacteria in the intestinal tract.

(2) In adults and infants, the chief clinical deficiency is increased bleeding tendencies. You should note that newborns have no intestinal bacteria and should be administered vitamin K. Prolonged use of broad-spectrum antibiotics or prolonged diarrhea may reduce the level of GI flora and result in a deficiency.

(3) In adults, K1 (phytonadione) overdoses, if given IV, may cause anaphylactic like reactions. K3 (menadione), in excess, can cause nausea, vomiting, and allergic reactions.

(4) K1 overdose in infants causes an increased level of bilirubin in the blood and severe hemolytic anemia. K3 overdose causes an increase in circulating blood in the brain with resultant brain damage or death. It is particularly hazardous in premature infants.

6-3. WATER-SOLUBLE VITAMINS

a. **Water-Soluble Vitamins.** Water-soluble vitamins are well absorbed from the small intestine by active transport in physiologic doses and by diffusion in large doses.

b. **Physiologic Doses.** In physiologic doses, these vitamins are distributed throughout the body with limited tissue storage. They are excreted as metabolites. In large doses, tissue saturation levels are rapidly reached, and the excess is excreted unchanged in the urine.

c. **Vitamin B1 (Thiamine).**

(1) Vitamin B1 is essential in the oxidation of keto-acids. Natural sources of vitamin B1 are lean meats, milk, fish, poultry, and grains.

(2) A deficiency of thiamin results in beriberi, which is characterized by GI disturbances, peripheral neurologic changes, and CNS depression. If cardiovascular effects (tachycardia, dyspnea on exertion, ECG abnormalities) occur, the condition is referred to as “cardiac beriberi.”

d. **Vitamin B2 (Riboflavin).**

(1) Vitamin B2 acts as a coenzyme for a variety of proteins and is found in milk, lean meats, egg, and yeast.

(2) A lack of this vitamin can cause sore throat and inflammation at the corner of the mouth. Later, inflammation of the tongue and seborrheic dermatosis may appear. B2 deficiency is difficult to recognize because it is similar to other vitamin deficiencies, and the symptoms are common signs of many diseases.

e. **Vitamin B6 (Pyridoxine).**

(1) Vitamin B6 acts as a coenzyme for metabolic transformation of amino acids, particularly the sulfur containing amino acids. Sources are meats, seafood, vegetables, and yeast.

(2) Deficiencies can cause seborrheic-like lesions about the eyes, nose, and mouth. Convulsive seizures may also be seen.

(3) Patients on INH (isoniazid) therapy require B6 supplementation because INH enhances its excretion.

f. **Vitamin B12 (Cyanocobalamin).**

(1) Vitamin B12 is essential for cell growth, replication, and maintenance of myelin throughout the nervous system. Meats, milk, and salt-water fish can provide Vitamin B12 through the diet.

(2) B12 deficiency causes pernicious anemia and may result in nerve damage due to inadequate myelin production.

g. **Folic Acid. (Folate).** Folic acid acts as a coenzyme in metabolic reactions in which there is a non-carbon unit transfer. Sources of folic acid are vegetables, meats, and yeast.

h. **Niacin (Nicotinic Acid, Nicotinamide).**

(1) Niacin acts as a coenzyme in the breakdown of glycogen, fat synthesis, and tissue respiration. Sources are bread, lean meat, liver, and yeast.

(2) Deficiency causes pellagra, which affects the skin, GI tract, or CNS. Reddening of the skin, like sunburn, first appears on the back of the hands. Other areas exposed to light are later affected and become widespread.

(3) Symptoms of the GI tract are inflammation of the mouth and stomach, causing diarrhea.The tongue becomes red and swollen (beefy tongue) and may ulcerate. Headache, dizziness, insomnia, depression, and loss of memory are signs of deficiency in the CNS.

i. **Pantothenic Acid.** Pantothenic acid is a precursor of coenzyme A, an enzyme that transports two-carbon groups in metabolism of fats, protein, and carbohydrates. Pantothenic acid is found in most food, so deficiency states are hard to demonstrate.

j. **Biotin.**

(1) Biotin acts as a coenzyme in the transport of carbon dioxide in fatty acid synthesis. Sources are meats, vegetables, and cereals.

(2) A deficiency state is difficult to demonstrate in man, but does include loss of hair, dermatitis, and loss of muscular control.

k. **Vitamin C (Ascorbic Acid).**

(1) Vitamin C plays a role in cellular respiration, the synthesis of collagen, and the absorption of iron from the gut. A few sources are citrus fruits, tomatoes, potatoes, and leafy foods.

(2) The deficiency state, scurvy, is mainly seen as a result of the failure to synthesize collagen. The gums become spongy and bleed easily. Capillary walls increase in fragility and hemorrhage when subjected to mechanical stress or trauma. Lesions of growing bones lead to disunion, freedom of movement, and traumatic fragmentation. Wound healing is also impaired.

6-4. MINERALS

a. **Mineral Needs.** As with vitamins, mineral needs vary from patient to patient, depending on their age, condition, and nutritional state. Some are needed in doses more than 100 mg a day, while others are needed in small amounts.

b. **Iron.** Iron is essential for oxygen transport and in enzyme systems concerned with electron transfer (cytochromes). Food sources that contain iron are organ meats, yeast, and wheat germ. A deficiency of iron results in anemia.

c. **Fluoride.** Fluoride occupies the anionic spaces in the enamel apatite crystal surface of teeth. How it retards dental caries (cavities) is not known. Sources of fluoride include plants and water. People who are deficient in fluoride suffer from excessive dental caries.

d. **Calcium.** Calcium is the fifth most abundant mineral in the body. It is present in more than 98 percent in the extracellular fluid and soft tissue. Calcium is essential in the formation of bone and for the coagulation of blood. It plays a central role in muscle contraction.

(1) Lack of calcium (hypocalcemia) may result in muscle cramps, tetany, convulsions, dyspnea, and personality changes.

(2) Excess calcium (hypercalcemia) may result in muscle weakness, thirst, anorexia, vomiting, constipation, stupor, and coma. Severe hypercalcemia may result in calcium deposits in the soft tissue of the body.

e. **Other Essential Minerals.** Other essential minerals include Phosphorus, Sodium, Zinc, Sulfur, Chlorine, Copper, Magnesium, Potassium, and Iodine.

Continue with Exercises

EXERCISES, LESSON 6

INSTRUCTIONS: Answer the following items by marking the lettered response that best answers the question or completes the statement.

After you have completed all these items, turn to "Solutions to Exercises" at the end of the lesson, and check your answers with the solutions.

For exercises 1 through 6, match the vitamin in Column I with its corresponding category in Column II.

Column I	Column II
1. Vitamin A	a. Water-soluble vitamin
2. Vitamin B12	b. Lipid (fat) soluble vitamin
3. Vitamin C	
4. Vitamin D	
5. Vitamin E	
6. Vitamin K	

7. Which of the following conditions is the result of niacin deficiency?

   a. Scurvy.

   b. Rickets.

   c. Pernicious anemia.

   d. Pellagra.

For exercises 8 through 12, match the vitamin/mineral in Column I with its corresponding function in Column II.

Column I	Column II
8. Iron	a. Embryonic development
9. Fluoride	b. Blood clotting
10. Vitamin A	c. Absorption of calcium
11. Vitamin E	d. Normal growth maintenance
12. Vitamin K	e. Tooth enamel
	f. Oxidation of Keto acids
	g. Oxygen transport

13. Which of the following conditions is the result of Vitamin C deficiency?

    a. Scurvy.

    b. Rickets.

    c. Pernicious anemia.

    d. Pellagra.

14. A toxicity associated with an overdose of Vitamin D is:

    a. Loss of appetite.

    b. Thrombophlebitis.

    c. Hypercalcemia.

    d. Alopecia.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 6

1. b (para 6-1c)
2. a (para 6-1c)
3. a (para 6-1c)
4. b (para 6-1c)
5. b (para 6-1c)
6. b (para 6-1c)
7. d (para 6-3h(2))
8. g (para 6-4b)
9. e (para 6-4c)
10. a (para 6-2c(1))
11. d (para 6-2e(1))
12. b (para 6-2f(1))
13. a (para 6-3k(2))
14. c (para 6-2d(5))

End of Lesson 6